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 NEWS  4  OCT 03  MATHDI removed from STN
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                  to core patent offices
 NEWS  6  OCT 13  New CAS Information Use Policies Effective October 17, 2005
 NEWS  7  OCT 17  STN(R) AnaVist(TM), Version 1.01, allows the export/download
                  of CAplus documents for use in third-party analysis and
                  visualization tools
 NEWS  8  OCT 27  Free KWIC format extended in full-text databases
 NEWS  9  OCT 27  DIOGENES content streamlined
 NEWS 10  OCT 27  EPFULL enhanced with additional content
 NEWS 11  NOV 14  CA/CAplus - Expanded coverage of German academic research
 NEWS 12  NOV 30  REGISTRY/ZREGISTRY on STN(R) enhanced with experimental
                  spectral property data
 NEWS 13  DEC 05  CASREACT(R) - Over 10 million reactions available

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L1            1 WO2002089809/PN
                (WO2002089809/PN)

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ENTER ANSWER NUMBER OR RANGE (1-):1
ENTER DISPLAY CODE (TI) OR ?:rn
E1 THROUGH E65 ASSIGNED

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E22           1     31523-22-5/BI
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E59           1     79-19-6/BI
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             2 173213-31-5/BI
           110 2215-33-0/BI
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             1 302954-63-8/BI
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         15 63286-28-2/BI
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          5 63894-54-2/BI
       1706 66-72-8/BI
       1555 708-06-5/BI
         42 7385-99-1/BI
         34 7727-07-3/BI
       3422 79-19-6/BI
          6 80751-35-5/BI
         16 87877-49-4/BI
         19 89570-82-1/BI
      11048 90-02-8/BI
       2519 91-56-5/BI
       1204 95-01-2/BI
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             OR 7385-99-1/BI OR 7727-07-3/BI OR 79-1

=> s l2 and (anemia or renal failure or hypoxia)
       34938 ANEMIA
        1848 ANEMIAS
       35302 ANEMIA
             (ANEMIA OR ANEMIAS)
      141226 RENAL
          10 RENALS
      141231 RENAL
             (RENAL OR RENALS)
      174777 FAILURE
       15133 FAILURES
      184336 FAILURE
             (FAILURE OR FAILURES)
       14678 RENAL FAILURE
             (RENAL(W)FAILURE)
       39090 HYPOXIA
          23 HYPOXIAS
       39091 HYPOXIA
             (HYPOXIA OR HYPOXIAS)
L3     4840 L2 AND (ANEMIA OR RENAL FAILURE OR HYPOXIA)

=> s s e60-62, e57-58, e53, e48-50, e29-e45, e19-26, e11-15, e3
MISSING OPERATOR 'S (80751-35-5'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s  e60-62, e57-58, e53, e48-50, e29-e45, e19-26, e11-15, e3
          6 80751-35-5/BI
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          16 87877-49-4/BI
          19 89570-82-1/BI
          42 7385-99-1/BI
          34 7727-07-3/BI
           2 63711-22-8/BI
          20 58333-11-2/BI
           9 59473-50-6/BI
          87 614-65-3/BI
           1 416885-82-0/BI
          20 4231-74-7/BI
           2 474787-56-9/BI
           1 474787-57-0/BI
           1 474787-58-1/BI
           1 474787-59-2/BI
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           1 474787-70-7/BI
          20 2824-60-4/BI
          35 28668-95-3/BI
           1 302954-63-8/BI
          39 31523-22-5/BI
           1 324031-29-0/BI
           1 330645-61-9/BI
           1 330980-90-0/BI
           1 341942-20-9/BI
           2 157592-75-1/BI
         106 15793-77-8/BI
          10 16111-50-5/BI
         138 17284-97-8/BI
           2 173213-31-5/BI
           3 111781-93-2/BI
L4       538 (80751-35-5/BI OR 87877-49-4/BI OR 89570-82-1/BI OR  7385-99-1/B
             I OR 7727-07-3/BI OR  63711-22-8/BI OR  58333-11-2/BI OR 59473-5
             0-6/BI OR 614-65-3/BI OR  416885-82-0/BI OR 4231-74-7/BI OR
             474787-56-9/BI OR 474787-57-0/BI OR 474787-58-1/BI OR 474787-59-
             2/BI OR 474787-60-5/BI OR 474787-61-6/BI OR 474787-62-7/BI OR
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             474787-70-7/BI OR  2824-60-4/BI OR 28668-95-3/BI OR 302954-63-8/
             BI OR 31523-22-5/BI OR 324031-29-0/BI OR 330645-61-9/BI OR 33098
             0-90-0/BI OR 341942-20-9/BI OR  157592-75-1/BI OR 15793-77-8/BI
             OR 16111-50-5/BI OR 17284-97-8/BI OR 173213-31-5/BI OR  111781-9
             3-2/BI)

=> s l3 and l4
L5         0 L3 AND L4

=> s l4 and (erythropoietin or red blood cell or erythroid or epo or erythropoiesis or erythro?
)
      12081 ERYTHROPOIETIN
        529 ERYTHROPOIETINS
      12114 ERYTHROPOIETIN
              (ERYTHROPOIETIN OR ERYTHROPOIETINS)
     375513 RED
        497 REDS
     375767 RED
              (RED OR REDS)
    1216590 BLOOD
       1208 BLOODS
    1216723 BLOOD
              (BLOOD OR BLOODS)
```

```
       1992499 CELL
       1752307 CELLS
       2646464 CELL
                 (CELL OR CELLS)
         33620 RED BLOOD CELL
                 (RED(W)BLOOD(W)CELL)
         11826 ERYTHROID
            34 ERYTHROIDS
         11837 ERYTHROID
                 (ERYTHROID OR ERYTHROIDS)
          6070 EPO
           135 EPOS
          6177 EPO
                 (EPO OR EPOS)
          8647 ERYTHROPOIESIS
        193603 ERYTHRO?
L6           1 L4 AND (ERYTHROPOIETIN OR RED BLOOD CELL OR ERYTHROID OR EPO OR
               ERYTHROPOIESIS OR ERYTHRO? )

=> s l4 and (anemia or anemic or renal failure or hypoxic or hypoxia)
         34938 ANEMIA
          1848 ANEMIAS
         35302 ANEMIA
                 (ANEMIA OR ANEMIAS)
          4383 ANEMIC
            34 ANEMICS
          4407 ANEMIC
                 (ANEMIC OR ANEMICS)
        141226 RENAL
            10 RENALS
        141231 RENAL
                 (RENAL OR RENALS)
        174777 FAILURE
         15133 FAILURES
        184336 FAILURE
                 (FAILURE OR FAILURES)
         14678 RENAL FAILURE
                 (RENAL(W)FAILURE)
         18494 HYPOXIC
             2 HYPOXICS
         18494 HYPOXIC
                 (HYPOXIC OR HYPOXICS)
         39090 HYPOXIA
            23 HYPOXIAS
         39091 HYPOXIA
                 (HYPOXIA OR HYPOXIAS)
L7           0 L4 AND (ANEMIA OR ANEMIC OR RENAL FAILURE OR HYPOXIC OR HYPOXIA)

=> d ibib abs it l6

L6   ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2002:868743  CAPLUS
DOCUMENT NUMBER:          137:352894
TITLE:                    Preparation of hydrazones and hydrazines for use in
                          increasing erythropoietin and
                          vascularization of tissue
INVENTOR(S):              Almstead, Ji-In Kim; Izzo, Nicholas John; Jones, David
                          Robert
PATENT ASSIGNEE(S):       The Procter & Gamble Company, USA
SOURCE:                   PCT Int. Appl., 53 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
     WO 2002089809        A1    20021114    WO 2002-US14106         20020506
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W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003092716	A1	20030515	US 2002-134890	20020429
US 6660737	B2	20031209		
US 2004053977	A1	20040318	US 2003-661905	20030912
PRIORITY APPLN. INFO.:			US 2001-288765P	P 20010504
			US 2002-134890	A3 20020429

OTHER SOURCE(S): MARPAT 137:352894

AB R1R2R3CNR4NR5R6 [R1, R6 = aryl, cycloalkyl, heteroaryl, heterocycloalkyl; R2, R4 = bond; R2, R4 = H; R3 = H, alkyl] were prepared for use as VEGF stimulators in increasing **erythropoietin** and vascularization of tissue. Thus, 2-acetylpyridine was treated with 2-hydrazinopyridine to give the hydrazone which had EC50 for induction of VEGF formation of 0.65 (no units).

IT Blood vessel
Human
(preparation of pyridyl hydrazones and hydrazines for use in increasing **erythropoietin** and vascularization of tissue)

IT 11096-26-7, **Erythropoietin** 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of pyridyl hydrazones and hydrazines for use in increasing **erythropoietin** and vascularization of tissue)

IT 2215-33-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyridyl hydrazones and hydrazines for use in increasing **erythropoietin** and vascularization of tissue)

IT **614-65-3P 2824-60-4P** 3788-81-6P **7385-99-1P**
7727-07-3P 16111-50-5P 58333-11-2P
59473-50-6P 63711-22-8P 87877-49-4P
111781-93-2P 157592-75-1P 173213-31-5P
302954-63-8P 324031-29-0P 330645-61-9P
330980-90-0P 341942-20-9P 416885-82-0P
474787-56-9P 474787-57-0P 474787-58-1P
474787-59-2P 474787-60-5P 474787-61-6P
474787-62-7P 474787-63-8P 474787-65-0P
474787-66-1P 474787-67-2P 474787-68-3P
474787-69-4P 474787-70-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridyl hydrazones and hydrazines for use in increasing **erythropoietin** and vascularization of tissue)

IT 66-72-8 79-19-6, Thiosemicarbazide 90-02-8, Salicylaldehyde, reactions 91-56-5, 2,3-Indoledione 95-01-2, 2,4-Dihydroxybenzaldehyde 100-63-0, Phenylhydrazine 139-85-5, 3,4-Dihydroxybenzaldehyde 148-53-8, 2-Hydroxy-3-methoxybenzaldehyde 368-90-1, 4-Trifluoromethylphenylhydrazine 529-20-4, o-Tolualdehyde 615-21-4, 2-Benzothiazolylhydrazine 708-06-5, 2-Hydroxy-1-naphthaldehyde 1121-60-4, 2-Pyridinecarboxaldehyde 1122-62-9, 2-Acetylpyridine 1122-72-1, 6-Methyl-2-pyridinecarboxaldehyde **4231-74-7**, N-Methyl-N-2-pyridylhydrazine 4930-98-7, 2-Hydrazinopyridine **15793-77-8**, 2-Quinolylhydrazine **17284-97-8**, 6-Chloro-3-pyridazinylhydrazine 23906-13-0, 4,6-Dimethyl-2-pyrimidinylhydrazine 63286-28-2 63894-54-2 **80751-35-5** **89570-82-1** 138949-13-0 241488-23-3, 5,7-Bis(trifluoromethyl)-1,8-naphthyridin-2-ylhydrazine **474787-64-9**, 8-Hydroxy-3-isoquinolinecarboxaldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of pyridyl hydrazones and hydrazines for use in increasing **erythropoietin** and vascularization of tissue)

IT **28668-95-3P 31523-22-5P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of pyridyl hydrazones and hydrazines for use in increasing **erythropoietin** and vascularization of tissue)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 1 ANSWERS CAPLUS COPYRIGHT 2005 ACS on STN
IC ICM A61K031-53
ICS A61P009-00; A61P013-12; A61P025-00; A61P043-00
CC 27-16 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
TI Preparation of hydrazones and hydrazines for use in increasing erythropoietin and vascularization of tissue
ST pyridyl hydrazone prepn VEGF erythropoietin vascularization stimulant
IT Blood vessel
Human
(preparation of pyridyl hydrazones and hydrazines for use in increasing erythropoietin and vascularization of tissue)
IT 11096-26-7, Erythropoietin 127464-60-2, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of pyridyl hydrazones and hydrazines for use in increasing erythropoietin and vascularization of tissue)
IT 2215-33-0P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of pyridyl hydrazones and hydrazines for use in increasing erythropoietin and vascularization of tissue)
IT 614-65-3P 2824-60-4P 3788-81-6P 7385-99-1P 7727-07-3P
16111-50-5P 58333-11-2P 59473-50-6P 63711-22-8P 87877-49-4P
111781-93-2P 157592-75-1P 173213-31-5P 302954-63-8P 324031-29-0P
330645-61-9P 330980-90-0P 341942-20-9P 416885-82-0P 474787-56-9P
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474787-62-7P 474787-63-8P 474787-65-0P 474787-66-1P 474787-67-2P
474787-68-3P 474787-69-4P 474787-70-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of pyridyl hydrazones and hydrazines for use in increasing erythropoietin and vascularization of tissue)
IT 66-72-8 79-19-6, Thiosemicarbazide 90-02-8, Salicylaldehyde, reactions
91-56-5, 2,3-Indoledione 95-01-2, 2,4-Dihydroxybenzaldehyde 100-63-0, Phenylhydrazine 139-85-5, 3,4-Dihydroxybenzaldehyde 148-53-8, 2-Hydroxy-3-methoxybenzaldehyde 368-90-1, 4-Trifluoromethylphenylhydrazine 529-20-4, o-Tolualdehyde 615-21-4, 2-Benzothiazolylhydrazine 708-06-5, 2-Hydroxy-1-naphthaldehyde 1121-60-4, 2-Pyridinecarboxaldehyde 1122-62-9, 2-Acetylpyridine 1122-72-1, 6-Methyl-2-pyridinecarboxaldehyde 4231-74-7, N-Methyl-N-2-pyridylhydrazine 4930-98-7, 2-Hydrazinopyridine 15793-77-8, 2-Quinolylhydrazine 17284-97-8, 6-Chloro-3-pyridazinylhydrazine 23906-13-0, 4,6-Dimethyl-2-pyrimidinylhydrazine 63286-28-2 63894-54-2 80751-35-5 89570-82-1 138949-13-0 241488-23-3, 5,7-Bis(trifluoromethyl)-1,8-naphthyridin-2-ylhydrazine 474787-64-9, 8-Hydroxy-3-isoquinolinecarboxaldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of pyridyl hydrazones and hydrazines for use in increasing erythropoietin and vascularization of tissue)
IT 28668-95-3P 31523-22-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of pyridyl hydrazones and hydrazines for use in increasing erythropoietin and vascularization of tissue)

ALL ANSWERS HAVE BEEN SCANNED

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     (FILE 'HOME' ENTERED AT 20:27:10 ON 08 DEC 2005)

     FILE 'CAPLUS' ENTERED AT 20:27:20 ON 08 DEC 2005
L1             0 S US2002089809A1/PN
L2             0 S US2002089809/PN
L3             1 S WO2002089809/PN
                 SELECT L3 1 RN
L4            73 S E29-E45, E21-26, E53, E48-E49, E3, 614-65-3/RN OR E2824-60-R/
L5             0 S L4 AND (ERYTHOROPOIETIN OR ERYTHROID COLONY STIMULATING ACTIV
L6             0 S L4 AND (ERYTHOROPOIETIN OR ERYTHROID OR ERYTHROPOIESIS OR ECS
L7           154 S (HYDRAZINE OR HYDRA?) AND (ERYTHOROPOIETIN OR ERYTHROID OR ER
L8           154 FOCUS L7 1-
L9           154 FOCUS L8 1-
                 SELECT L3 1 RN
L10         1078 S 1-130
L11        59900 S E1-E130
L12         5380 S L11 AND (ERYTHOROPOIETIN OR ERYTHROID OR ERYTHROPOIESIS OR EC
L13           38 S (HYDRAZINE OR HYDRA?) AND L12
L14           38 FOCUS L13 1-

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L8 ANSWER 9 OF 154 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:252250 CAPLUS
DOCUMENT NUMBER: 124:290579
TITLE: N,N-dimethyl-N,N-diallylammonium chloride copolymers with acrylic acid and 2-(4-hydroxy-3,5-di-tert-butylphenyl)ethylcarbonyl acrylic **hydrazide** as γ radiation-induced mutation inhibitors and **erythropoiesis** stimulants
INVENTOR(S): Shevchenko, Vladimir A.; Topchiev, Dmitrij A.; Aleksandrova, Valentina A.; Kotlyarova, Elena B.; Odin, Andrej P.; Domnina, Nina S.
PATENT ASSIGNEE(S): Russia
SOURCE: Russ. From: Izobreteniya 1995, (25), 163-4.
CODEN: RUXXE7
DOCUMENT TYPE: Patent
LANGUAGE: Russian
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
RU 2043368	C1	19950910	RU 1992-5249	19921113

PRIORITY APPLN. INFO.: RU 1992-5249 19921113
AB Title only translated.

L8 ANSWER 10 OF 154 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1973:156882 CAPLUS
DOCUMENT NUMBER: 78:156882
TITLE: **Erythropoiesis** in the newt, Triturus cristatus. II. Characteristics of the erythropoietic process
AUTHOR(S): Grasso, J. A.
CORPORATE SOURCE: Sch. Med., Boston Univ., Boston, MA, USA
SOURCE: Journal of Cell Science (1973), 12(2), 491-523
CODEN: JNCSAI; ISSN: 0021-9533
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In splenectomized newts (Triturus cristatus) rendered anemic by acetylphenyl **hydrazine** (I), an erythropoietic response was delayed so that the animals were completely devoid of erythron, including erythrocytes. At 11-14 days after I treatment, **erythroid** precursor cells (EPC) in the blood signaled the occurrence of an erythropoietic response. Ultrastructural studies showed few or no ribosomes in EPC, but well developed nucleoli and intense RNA synthesis were seen in these cells. Correlated morphol. and cytochem. data indicated the production of ribosomes in EPC with eventual formation of basophilic erythroblasts (BE). Microphotometric studies showed accumulation of heme during this interval. Thus, in EPC and BE, both rRNA and mRNA were synthesized, making possible the early synthesis of Hb. In subsequent stages, nucleoli exhibited a size decrease, while all RNA ceased during the midpolychromatophilic erythroblast (MPE) stage. Coupled with the gradual loss of ribosomes, rRNA synthesis occurred in EPC, BE, and early MPE where it was completed. Hb mRNA was also formed in these stages. Beyond MPE, Hb production was dependent on stable mRNA since no RNA synthesis was detected in this period. Autophagy played a role in the loss of cytoplasmic organelles in the erythropoietic process.

L8 ANSWER 4 OF 154 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:189483 CAPLUS
DOCUMENT NUMBER: 126:187152
TITLE: Finely powdered **hydrazide** compounds as crosslinking agents for heat- and moisture-resistant epoxy resin sealants
INVENTOR(S): Kamya, Kazusaki; Hayashi, Hiroyasu; Maekawa, Tsukasa
PATENT ASSIGNEE(S): Otsuka Kagaku Kk, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09003021	A2	19970107	JP 1995-150054	19950616
PRIORITY APPLN. INFO.:			JP 1995-150054	19950616

AB The compds. are finely powdered **hydrazide** compds. containing ≥1 **hydrazide** group per mol. (average particle size 0.5-20 μm). The compds. are especially useful for epoxy resin sealants for packaging of electronic parts, e.g. liquid crystal display devices. Thus, a composition containing 100 parts **Epo** Tohto YD 128 (epoxy resin) and 30 parts finely powdered adipic acid dihydrazide (average particle size 2.0 μm) showed gel time 10 min (at 120°) and gave a test piece with good heat and moisture resistance.

L8 ANSWER 5 OF 154 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:634955 CAPLUS
DOCUMENT NUMBER: 125:266017
TITLE: Use of hcp specific compounds to enhance **erythropoiesis**
INVENTOR(S): Dunnington, Damien John
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: Eur. Pat. Appl., 46 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 728482	A2	19960828	EP 1996-200269	19960207
EP 728482	A3	19991020		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
AU 9644405	A1	19960822	AU 1996-44405	19960207
ZA 9601000	A	19960807	ZA 1996-1000	19960208
CA 2169132	AA	19960811	CA 1996-2169132	19960208
ZA 9601001	A	19960813	ZA 1996-1001	19960208
CN 1135333	A	19961113	CN 1996-104364	19960208
CN 1137378	A	19961211	CN 1996-105740	19960208
JP 09002974	A2	19970107	JP 1996-59922	19960208
CA 2212645	AA	19960815	CA 1996-2212645	19960209
WO 9624343	A1	19960815	WO 1996-US1964	19960209
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, PT, RO, RU, SD, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9649237	A1	19960827	AU 1996-49237	19960209
EP 809490	A1	19971203	EP 1996-905494	19960209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
BR 9607614	A	19980609	BR 1996-7614	19960209
JP 10513474	T2	19981222	JP 1996-524486	19960209

WO 9624847	A1	19960815	WO 1996-US2490	19960212
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 811159	A1	19971210	EP 1996-906615	19960212
R: BE, CH, DE, DK, FR, GB, IT, LI, NL				
JP 10513564	T2	19981222	JP 1996-524493	19960212
ZA 9601318	A	19970127	ZA 1996-1318	19960220
ZA 9605499	A	19980330	ZA 1996-5499	19960628
ZA 9605500	A	19980330	ZA 1996-5500	19960628
FI 9703259	A	19971008	FI 1997-3259	19970807
NO 9703659	A	19971008	NO 1997-3659	19970808

PRIORITY APPLN. INFO.:	US 1995-386381	A 19950210
	US 1995-400220	A 19950307
	US 1995-497357	A 19950630
	US 1995-540680	A 19951011
	US 1995-581089	A 19951229
	WO 1996-US1964	W 19960209
	WO 1996-US2490	W 19960212

AB Invented is a method of enhancing **erythropoiesis** in a subject which comprises administering to the subject a therapeutically effective amount of a compound which binds to the human hcp SH2 domain with a binding affinity greater than fifty-fold higher than the binding affinity with which the compound binds to a human SH-PTP2 SH2 domain, and, binds to a human src SH2 domain, a human lck SH2 domain, a human fyn SH2 domain and a human p85 SH2 domain with a binding affinity which is greater than fifty-fold lower than the binding affinity with which the compound binds to such hcp SH2 domain. Thus, Et 2-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate and Et 3-ethoxycrotonate in toluene were treated with camphorsulfonic acid and heated at reflux for 3 h. The mixt was cooled, concentrated, and the residue dissolved in Et acetate. Acetic acid was added, solvent evaporated, and the resulting solid triturated with MeOH to yield Et 4-hydroxy-2-methyl-5,6,7,8-tetrahydrobenzo[b]thieno[2,3-b]pyridine-2-carboxylate. This is refluxed in phosphorus oxychloride for 3.5 h. The phosphorus oxychloride was removed and the residual oil dissolved in Et acetate, washed and dried to produce Et 4-chloro-2-methyl-5,6,7,8-tetrahydrobenzo[b]thieno[2,3-b]pyridine-2-carboxylate. In MeOH this was treated with **hydrazine** monohydrate and heated at reflux for 16 h, poured over diluted aqueous HCl to precipitate 2,3,7,8,9,10-hexahydro-4-methyl-1H-benzo[b]thieno[2,3-b]pyrazolo[3,4-d]pyridin-3-one. Compds. of the invention were tested for binding affinity with peptides representing the protein domains listed above. In mice, L-3,5-dibromo-3'-(6-oxo-3(1H)-pyridazinylmethyl)thyronine increased reticulocyte counts at dosages from 200-800 mg/kg/day.

L8 ANSWER 2 OF 154 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1958:78667 CAPLUS
DOCUMENT NUMBER: 52:78667
ORIGINAL REFERENCE NO.: 52:13998h-i
TITLE: Influence of isonicotinoyl **hydrazide** on **erythropoiesis** and blood iron in children with tuberculosis
AUTHOR(S): Arditi, E.
CORPORATE SOURCE: Univ. Turin, Italy
SOURCE: Minerva Pediatrica (1956), 8, 1379-84
CODEN: MIPEA5; ISSN: 0026-4946
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 49, 6479c. In 20 patients the isonicotinoyl **hydrazide** treatment resulted in a progressive improvement of general conditions, of blood dyscrasias, and of total and serum Fe contents (I) of blood. The I increases were interpreted as a consequence of the decreased ferropexic activity of reticuloendothelium.

L14 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:247011 CAPLUS
DOCUMENT NUMBER: 140:276178
TITLE: Polypeptides conjugation with hydroxyalkyl starch for therapeutic uses
INVENTOR(S): Conradt, Harald S.; Grabenhorst, Eckart; Nimtz, Manfred; Zander, Norbert; Frank, Ronald; Eichner, Wolfram
PATENT ASSIGNEE(S): Fresenius Kabi Deutschland G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 50 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 8
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1400533	A1	20040324	EP 2002-20425	20020911
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
CA 2495242	AA	20040325	CA 2003-2495242	20030808
CA 2496317	AA	20040325	CA 2003-2496317	20030808
CA 2496318	AA	20040325	CA 2003-2496318	20030808
WO 2004024776	A1	20040325	WO 2003-EP8829	20030808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004024761	A1	20040325	WO 2003-EP8858	20030808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
WO 2004024777	A1	20040325	WO 2003-EP8859	20030808
WO 2004024777	C1	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
BR 2003014106	A	20050719	BR 2003-14106	20030808
BR 2003014107	A	20050719	BR 2003-14107	20030808
BR 2003014227	A	20051025	BR 2003-14227	20030808
EP 1398322	A1	20040317	EP 2003-20423	20030911
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
EP 1398327	A1	20040317	EP 2003-20424	20030911
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
EP 1398328	A1	20040317	EP 2003-20425	20030911

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 2005234230	A1	20051020	US 2005-77906		20050311
US 2005238723	A1	20051027	US 2005-78098		20050311
NO 2005001419	A	20050530	NO 2005-1419		20050317
NO 2005001418	A	20050531	NO 2005-1418		20050317
NO 2005001427	A	20050531	NO 2005-1427		20050317
PRIORITY APPLN. INFO.:			EP 2002-20425	A	20020911
			US 2002-409781P	P	20020911
			WO 2003-EP8829	W	20030808
			WO 2003-EP8858	W	20030808
			WO 2003-EP8859	W	20030808

AB The present invention relates to HAS-polypeptide conjugate (HAS-polypeptide) comprising one or more HAS mols., wherein each HAS is conjugated to the polypeptide via a carbohydrate moiety or a thioether, as well as to methods for the production thereof. In a preferred embodiment, the polypeptide is erythropoietin (**EPO**). For example,.

IT **11096-26-7DP**, Erythropoietin, conjugates with hydroxyalkyl starch
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(production of polypeptide conjugates with hydroxyalkyl starch for therapeutic uses)

IT **11096-26-7D**, Erythropoietin, thio/glyco derivs.
RL: RCT (Reactant); RACT (Reactant or reagent)
(production of polypeptide conjugates with hydroxyalkyl starch for therapeutic uses)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 19 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:354803 CAPLUS
DOCUMENT NUMBER: 140:350572
TITLE: Methods of using and compositions comprising immunomodulatory compounds for the treatment and management of myelodysplastic syndromes
INVENTOR(S): Zeldis, Jerome B.
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004035064	A1	20040429	WO 2003-US11323	20030413
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004220144	A1	20041104	US 2003-411649	20030411
CA 2477301	AA	20040429	CA 2003-2477301	20030413
EP 1487461	A1	20041222	EP 2003-726262	20030413
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003015315	A	20050816	BR 2003-15315	20030413
PRIORITY APPLN. INFO.:			US 2002-418468P	P 20021015
			WO 2003-US11323	W 20030413

OTHER SOURCE(S): MARPAT 140:350572

AB Methods of treating, preventing and/or managing myelodysplastic syndromes are disclosed. Specific methods encompass the administration of

immunomodulatory compound, or a pharmaceutically acceptable salt, solvate, **hydrate**, stereoisomer, clathrate, or prodrug thereof, alone or in combination with a second active ingredient, and/or the transplantation of blood or cells. Specific second active ingredients are capable of affecting or improving blood cell production Pharmaceutical compns., single unit dosage forms, and kits suitable for use in methods of the invention are also disclosed. Patients with myelodysplastic syndromes were treated orally with 3-(4-amino-1-oxo-1,3-dihydro-isoindol-2-yl)-piperidine-2,6-dione.

IT **11096-26-7, EPO**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as second active agent; immunomodulatory compds. and compns. for treatment and management of myelodysplastic syndromes)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 20 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:652540 CAPLUS
DOCUMENT NUMBER: 134:141451
TITLE: Plasma erythropoietin concentrations in patients receiving intensive platinum or nonplatinum chemotherapy
AUTHOR(S): Canaparo, R.; Casale, F.; Muntoni, E.; Zara, G. P.; Della Pepa, C.; Berno, E.; Pons, N.; Fornari, G.; Eandi, M.
CORPORATE SOURCE: Department of Anatomy, Pharmacology and Forensic Medicine, University of Turin, Turin, Italy
SOURCE: British Journal of Clinical Pharmacology (2000), 50(2), 146-153
CODEN: BCPHBM; ISSN: 0306-5251
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Platinum chemotherapy has been shown to have potent antineoplastic activity against various tumors, especially testicular, bladder, ovarian, head and neck cancers. This activity is accompanied by side-effects of nephrotoxicity and cumulative myelosuppression, the latter frequently presenting as severe anemia. Cisplatin and carboplatin nephrotoxicity might lower erythropoietin (**Epo**) secretion and, by this mechanism, contribute to the anemia that follows therapy with this chemotherapeutic agent. The aim of the present work is to study the plasma immunoerythropoietin and Hb levels of cancer patients treated with platinum or 5-fluorouracil-based chemotherapy. Plasma was obtained from 25 patients who were about to receive chemotherapy for advanced malignancy: 15 treated with cisplatin or carboplatin and 10 with nonplatinum drugs. Blood was collected on the first day (before drug administration) and around day 15 of every chemotherapy course. Complete blood count, creatinine and immunoreactive **Epo** levels were also measured in 22 healthy volunteers. An increase in **Epo** levels occurred following every course of 5-FU or platinum based chemotherapy in patients with steady concns. of creatinine and decreased levels of Hb. In particular, we observed an increase after about 15 days of the chemotherapy treatment and the **Epo** levels declined toward normal just before the following course. This phenomenon was evident in every course. Our results suggest that chemotherapy administration, using the current stds. of **hydration** and forced diuresis, slightly lowered Hb levels but did not depress **Epo** production, both in 5-FU and in platinum treated subjects.

IT **11096-26-7**, Erythropoietin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(plasma erythropoietin concns. in patients receiving intensive platinum or nonplatinum chemotherapy)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 21 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1965:447638 CAPLUS

DOCUMENT NUMBER: 63:47638
ORIGINAL REFERENCE NO.: 63:8689b-d
TITLE: Effect of massive triamcinolone administration in blunting the erythropoietic response to phenylhydrazine hemolysis
AUTHOR(S): Cohen, Phin; Gardner, Frank H.
CORPORATE SOURCE: Harvard Med. School, Boston, MA
SOURCE: Journal of Laboratory and Clinical Medicine (1965), 65(1), 88-101
CODEN: JLCMAK; ISSN: 0022-2143
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The simultaneous administration of acetylphenylhydrazine (I) and massive doses of triamcinolone (II) to rabbits prevented the elaboration of a maximum pulse of reticulocytes that was seen in rabbits given only I. Not only was the reticulocyte response blunted but it was also prolonged, so that the area under the reticulocyte curves of the 2 groups was equal. The recovery of hemoglobin (Hb) concu. was delayed in onset by 7 days and was incomplete in the II group. This suggested that II had caused a production deficit prolonging the Hb recovery by limiting the output of reticulocytes. Associated with the Hb, the II-treated only with I demonstrated a reduction in the percent of marrow fat when compared with controls. When massive II was added to this program, the percent of proximal (rib, humerus, femur) marrow fat was higher than in animals treated only with I.
IT **100-63-0, Hydrazine**, phenyl-
(**erythropoiesis** response to, triamcinolone inhibition of)

L14 ANSWER 22 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1957:48301 CAPLUS
DOCUMENT NUMBER: 51:48301
ORIGINAL REFERENCE NO.: 51:8975f-g
TITLE: Action of phenylhydrazine on the marrow of albino rats treated with aminopterin
AUTHOR(S): Calapso, P.
SOURCE: Excerpta Medica, Section 2: Physiology, Biochemistry and Pharmacology (1956), 9, 778
CODEN: EMPBA4; ISSN: 0014-4061
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Albino rats treated with large doses of aminopterin (I) and phenylhydrazine (II) did not show any change in medullary **erythropoiesis**. It is concluded that I in small doses does not affect marrow activity, while in larger doses it blocks activity and makes the marrow insensitive to the increased erythropoietic demands following the hemolysis produced by II. In animals so treated lymphocytes and eosinophils have a particular behavior, as in the cases of suprarenal deficit.
IT **100-63-0, Hydrazine**, phenyl-
(**erythropoiesis** after treatment with aminopterin and)

L14 ANSWER 23 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1957:48300 CAPLUS
DOCUMENT NUMBER: 51:48300
ORIGINAL REFERENCE NO.: 51:8975f-g
TITLE: Action of phenylhydrazine on the marrow of albino rats treated with aminopterin
AUTHOR(S): Calapso, P.
SOURCE: Archivio "E. Maragliano" di Patologia e Clinica (1955), 11, 171-82
CODEN: AMPCAV; ISSN: 0004-0193
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Albino rats treated with large doses of aminopterin (I) and phenylhydrazine (II) did not show any change in medullary **erythropoiesis**. It is concluded that I in small doses does not affect marrow activity, while in larger doses it blocks activity and makes the marrow insensitive to the increased erythropoietic demands following the hemolysis produced by II. In animals so treated lymphocytes and

eosinophils have a particular behavior, as in the cases of suprarenal deficit.
IT **100-63-0, Hydrazine**, phenyl-
(**erythropoiesis** after treatment with aminopterin and)

L14 ANSWER 24 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:487396 CAPLUS
DOCUMENT NUMBER: 143:205919
TITLE: Phase I Trial of Intravenous Cisplatin-Topotecan Chemotherapy for Three Consecutive Days in Patients with Advanced Solid Tumors: Parallel Topotecan Escalation in Two Fixed Platinum Dosing Schemes
AUTHOR(S): Pentheroudakis, G.; Briasoulis, E.; Karavassilis, V.; Mauri, D.; Tzamakou, E.; Rammou, D.; Pavlidis, N.
CORPORATE SOURCE: Department of Medical Oncology, University Hospital of Ioannina, Ioannina, Greece
SOURCE: Chemotherapy (Basel, Switzerland) (2005), 51(2-3), 154-161
CODEN: CHTHBK; ISSN: 0009-3157
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Purpose: We performed a phase I study of two fixed dosing schemes of cisplatin, a DNA cross-linker, with i.v. escalating topotecan, a DNA-topoisomerase I inhibitor. Exptl. Design: 40 patients with advanced solid tumors received i.v. cisplatin at a fixed dose of either 25 mg/m2 (schedule A) or 20 mg/m2 (schedule B) daily for 3 days with standard **hydration**. Topotecan escalation proceeded in 0.75, 0.90, 1.0, 1.15 mg/m2 cohorts in schedule A and 1.0, 1.1, 1.2, 1.3 mg/m2 cohorts in schedule B, administered i.v. at the end of cisplatin infusion daily for 3 days, repeated every 3 wk. Dose-limiting toxicity (DLT) consisted of protracted grade IV neutropenia, febrile neutropenia, grade IV thrombocytopenia and any grade III/IV non-hematol. toxicity. **Epoetin** and granulocyte colony-stimulating factor support was allowed on severe myeloablation. Endpoints were the identification of maximal tolerated dose (MTD), DLT and other toxicity. Results: The MTD was reached in cohort 25/1.15 mg/m2 in schedule A and 20/1.2 mg/m2 in schedule B. All DLT seen consisted of three episodes of febrile neutropenia and two of grade IV thrombocytopenia in schedule A, with three episodes of febrile neutropenia and one of protracted neutropenia in schedule B. Myelosuppression was substantial in all cohorts despite granulocyte colony-stimulating factor and **epoetin** support, peaked on the third week of treatment and resulted in administration of chemotherapy at a median of every 4 wk. Non-hematol. toxicity was mild. The response rate was 51% with seven complete responses occurring in patients with ovarian cancer, small cell and non-small cell lung cancer and cancer of unknown primary. The recommended dose was 20/ 1.1 mg/m2 for cisplatin and topotecan on schedule B, as the number of responses and administered topotecan dose were higher in schedule B recommended dose with lower cisplatin dose, minimizing problems of nephrotoxicity and vomiting. Conclusions: The schedule B daily cisplatin-topotecan + 3 combination with secondary cytokine support is associated with promising activity and schedule convenience. However, substantial myelosuppression undermines its applicability in the palliative setting, stressing the need for less toxic regimens.
IT **11096-26-7, Epoetin**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**Epoetin**; cisplatin-topotecan chemotherapy with secondary cytokine support for three consecutive days in patients with advanced solid tumors)
REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 25 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:965013 CAPLUS
DOCUMENT NUMBER: 141:406144
TITLE: Methods for treating degenerative diseases/injuries using nonpeptide thrombopoietin receptor agonists

INVENTOR(S): Erickson-Miller, Connie L.; Jenkins, Julian
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004096154	A2	20041111	WO 2004-US13468	20040429
WO 2004096154	A3	20050331		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2003-466540P	P	20030429
US 2003-471554P	P	20030519
US 2003-495034P	P	20030814
US 2004-549977P	P	20040304
US 2004-554581P	P	20040319
US 2004-556390P	P	20040325

OTHER SOURCE(S): MARPAT 141:406144

AB Invented is a method of treating degenerative diseases/injuries, in a mammal, including a human, in need thereof which comprises the administration of a therapeutically effective amount of a non-peptide TPO receptor agonist to such mammal. An injectable form for administering the present invention is produced by stirring 1.5 % by weight of 4'-[N'-[1-(3,4-dimethylphenyl)-3-methyl-5-oxo-1,5-dihydropyrazol-4-ylidene]**hydrazino**]-3'-hydroxy biphenyl-3-carboxylic acid in 10 % by volume propylene glycol in water.

IT **11096-26-7, EPO**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-administration of; nonpeptide thrombopoietin receptor agonists for treatment of degenerative diseases/injuries)

L14 ANSWER 26 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:665423 CAPLUS
DOCUMENT NUMBER: 123:65662
TITLE: Vitamin B12 Mediated Oral Delivery Systems for Granulocyte-Colony Stimulating Factor and Erythropoietin
AUTHOR(S): Russell-Jones, G. J.; Westwood, S. W.; Habberfield, A. D.
CORPORATE SOURCE: Biotech Australia Pty Ltd., Roseville, 2069, Australia
SOURCE: Bioconjugate Chemistry (1995), 6(4), 459-65
CODEN: BCCHES; ISSN: 1043-1802
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB As a prelude to the development of orally active erythropoietin (**EPO**) and granulocyte-colony stimulating factor (G-CSF), conjugates have been formed between these mols. and vitamin B12. During the formation of these conjugates intramol. crosslinking of the proteins was avoided by the use of **hydrazidyl** derivs. of vitamin B12. A potentially biodegradable linkage was formed between vitamin B12 and G-CSF by reaction of the buried thiol in G-CSF with a long chain dithio-pyridyl derivative of vitamin B12. In vitro and in vivo testing of the conjugates showed that their bioactivity was substantially maintained and that they were actively transported in an intrinsic factor dependent fashion across

CaCo-2 cells and from the intestine to the circulation in a biol. active form.

IT **11096-26-7DP**, Erythropoietin, reaction products with vitamin B12 derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(vitamin B12 mediated oral delivery systems for granulocyte-colony stimulating factor and erythropoietin)

L14 ANSWER 27 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:676600 CAPLUS
DOCUMENT NUMBER: 135:236432
TITLE: Methods and formulations containing secretory phospholipase A2 (sPLA2) inhibitors for the treatment of renal dysfunction
INVENTOR(S): Macias, William Louis; Meador, Vincent Phillip
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 161 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001066110	A2	20010913	WO 2001-US7	20010116
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1265607	A2	20021218	EP 2001-956186	20010116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003525901	T2	20030902	JP 2001-564763	20010116
US 2003087944	A1	20030508	US 2002-203436	20020805
PRIORITY APPLN. INFO.:			US 2000-188039P P	20000309
			WO 2001-US7 W	20010116

OTHER SOURCE(S): MARPAT 135:236432
AB A method is disclosed for the treatment of symptoms associated with renal dysfunction by administering to an animal in need thereof a therapeutically effective amount of a sPLA2 inhibitor, e.g. a 1H-indole-3-glyoxylamide. Preparation of [(3-(2-Amino-1,2-dioxoethyl)-2-ethyl-1-(phenylmethyl)-1H-indol-4-yl)oxy]acetic acid is described.
IT **11096-26-7**, Erythropoietin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(secretory phospholipase A2 inhibitors for treatment of renal dysfunction)

L14 ANSWER 28 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1959:68595 CAPLUS
DOCUMENT NUMBER: 53:68595
ORIGINAL REFERENCE NO.: 53:12480f-h
TITLE: Influence of phenylhydrazine on the blood level of siderophilin and iron in rabbits
AUTHOR(S): Schade, A. L.; Stengle, J. M.
CORPORATE SOURCE: Natl. Insts. of Health, Bethesda, MD
SOURCE: Naunyn-Schmiedebergs Archiv fuer Experimentelle Pathologie und Pharmakologie (1959), 236, 69-71
CODEN: AEPPAE; ISSN: 0365-2009
DOCUMENT TYPE: Journal

LANGUAGE: Unavailable
AB Phenylhydrazine has an inhibiting effect on the formation of erythrocytes and apparently suppresses the stimulation of the bone marrow to build new erythrocytes. The bilirubin level in rabbits varies normally between 44 and 90 γ%. Daily injection with 8-12 mg. acetylphenylhydrazine/kg. for 4 days caused considerable increases up to 300 γ % on the 5th day. The siderophilin values of the treated animals increased after the end of treatment obtaining a maximum of 150% of the initial level. Lack of hemoglobin led to a decrease in the blood Fe level and in normal conditions of alimentation to increased siderophilin values. Electrophoresis of the serum showed no changes in the α-, β2, and γ-fractions but marked changes in the albumin and β1-fraction.
IT **100-63-0, Hydrazine**, phenyl-
(effect on proteins in blood)

L14 ANSWER 29 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1959:68594 CAPLUS
DOCUMENT NUMBER: 53:68594
ORIGINAL REFERENCE NO.: 53:12480d-f
TITLE: Influence of phenylhydrazine on the erythrocyte metabolism in vivo
AUTHOR(S): Stopp, G.
CORPORATE SOURCE: Humboldt Univ., Berlin
SOURCE: Naunyn-Schmiedebergs Archiv fuer Experimentelle Pathologie und Pharmakologie (1959), 236, 67-8
CODEN: AEPPAE; ISSN: 0365-2009
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Phenylhydrazine-treated erythrocytes form not only lactic acid but also pyruvic acid. By adding in graded doses PhNHNH2Cl of 0 to 500 mg. % to a suspension of 109 cells/ml. it was shown that damage to the lactic dehydrogenase system appears only at a concentration of about 2.76 + 10-15 moles/cell (normal hemoglobin content of 2 + 10-15 valences/cell). The dehydrogenation of lactic acid to pyruvic acid occurs in aerobic and anaerobic conditions in cell suspensions, and in nicotinamide protected stroma-free hemolyzates, but not in suspensions of stroma. There exists therefore in the phenylhydrazine-treated cells a H-acceptor. At high doses, there occurs in addition damage to the enzyme system. The H-acceptor is not methemoglobin.
IT **100-63-0, Hydrazine**, phenyl-
(effect on erythrocyte metabolism)

L14 ANSWER 30 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1963:470296 CAPLUS
DOCUMENT NUMBER: 59:70296
ORIGINAL REFERENCE NO.: 59:13086f-h
TITLE: Tissue globulin importance for development of toxemia after irradiation
AUTHOR(S): Balika, Yu. D.; L'vitsyna, G. M.
SOURCE: Radiobiologiya (1963), 3(4), 529-34
CODEN: RADOA8; ISSN: 0033-8192
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. CA 58, 10494b. Tissue γ-globulins (I) were prepared from legs of dogs before and after wholebody irradiation (800 r.). Biol. properties of irradiated and nonirradiated I were studied in vitro and in vivo. irradiated I possessed a strong leukolytic activity in expts. in vitro. Both irradiated and nonirradiated I caused changes in leukocyte number after injection in healthy dogs: 3 hrs. after injection the number of leukocytes was reduced in both cases, after 6 hrs. it was at the initial level, and after 24 hrs. an increase in the number of leukocytes was found (up to 170% with irradiated I, and to 210% with nonirradiated I). In the bone marrow the number of erythroblasts and the regenerative index were reduced after injection of irradiated I. Phagocytic activity of blood neutrophils was at the same level up to 3 days after any I injection; then decreased activity was observed in the case of irradiated I. Bactericidal activity of skin and **erythropoiesis** were also reduced. I from irradiated tissue was suggested to be one of toxic factors which influence the course

of radiation sickness.
IT **100-63-0, Hydrazine**, phenyl-
(hemopoiesis response to, in radiation sickness)

L14 ANSWER 31 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1955:43220 CAPLUS
DOCUMENT NUMBER: 49:43220
ORIGINAL REFERENCE NO.: 49:8352f-i,8353a
TITLE: Some biological aspects of the factor in bone marrow responsible for hematopoietic recovery following systemic irradiation
AUTHOR(S): Brown, Mary B.; Hirsch, Barbara B.; Nagareda, C. Susan; Hochstetler, Sarah K.; Faraghan, Wm. G.; Toch, Paul; Kaplan, Henry S.
CORPORATE SOURCE: Stanford Univ. School of Med., San Francisco, CA
SOURCE: Journal of the National Cancer Institute (1940-1978) (1955), 15, 949-73
CODEN: JNCIAM; ISSN: 0027-8874
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB cf. C.A. 48, 858e, following abstrs. Thymic weight 50 days after the start of fractional total-body irradiation was used as an assay in strain C57BL mice to study the nature and mode of action of the material in mouse bone marrow, which reduces mortality, promotes hematopoietic regeneration, and inhibits lymphoid-tumor development in irradiated mice. Marrow cells enclosed in intraperitoneal capsules with a porous end-window did not elaborate a humoral material capable of diffusing from the capsule to act on the host. Differentially centrifuged mouse bone marrow and spleen cells showed activity in the nuclear fraction. The cytoplasmic and supernatant fractions were entirely inactive. The effect of thigh-shielding does not depend upon the presence of the spleen. Pretreatment of donor mice with phenylhydrazine or turpentine elicited an intense hyperplasia of the **erythroid** or myeloid cellular elements, resp., of the marrow and spleen, but did not modify activity in the thymic-weight assay. The active factor is in the more primitive cells of the marrow and spleen. With the exception of fetal liver, all adult and fetal tissues other than marrow and young spleen were inactive. Marrow from strain A mice and from rats was inactive. Homologous marrow incubated in vitro with P32 and injected intravenously was distributed primarily in the reticuloendothelial tissues, with little in the thymus or blood. Most of the injected activity could not be accounted for. Freezing or lyophilization inactivated the marrow.
IT **100-63-0, Hydrazine**, phenyl-
(effect on bone marrow and spleen)

L14 ANSWER 32 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1954:50218 CAPLUS
DOCUMENT NUMBER: 48:50218
ORIGINAL REFERENCE NO.: 48:8930a-c
TITLE: The effect of splenectomy or phenylhydrazine on infections with Plasmodium berghei in the white mouse
AUTHOR(S): Singer, Ira
CORPORATE SOURCE: Christ Hosp. Inst. of Med. Research, Cincinnati, O.
SOURCE: Journal of Infectious Diseases (1954), 94, 159-63
CODEN: JIDIAQ; ISSN: 0022-1899
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Mice were splenectomized 2 days prior to infection or treated with 0.06 mg. per g. body weight phenylhydrazine-HCl or acetylphenylhydrazine. After the 6th day of infection, animals lacking spleens exhibited a lower parasitemia and lower reticulocyte count than the nephrectomized and unoperated controls. Drug-treated animals maintained a higher parasite count and more intense reticulocytosis through the course of infection than did control animals. The drugs did not affect the survival time. They apparently had no effect on the mechanisms of acquired immunity. These results are discussed in relation to changes in **erythroid** tissue which govern the ability of the host to supply substrate for the parasite and in relation to the parasites' preference for immature erythrocytes.

IT **100-63-0, Hydrazine**, phenyl-
(effect on Plasmodium berghei infection)

L14 ANSWER 33 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:136600 CAPLUS
DOCUMENT NUMBER: 142:241182
TITLE: Synthesis and application of branched polymer-peptide conjugates
INVENTOR(S): Behrens, Carsten; Doerwald, Florencio Zaragoza; Kofod-Hansen, Mikael; Lau, Jesper; Kodra, Janos Tibor; Hansen, Thomas Kruse; Bloch, Paw
PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014049	A2	20050217	WO 2004-DK531	20040809
WO 2005014049	A3	20050901		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

DK 2003-1145	A	20030808
US 2003-494447P	P	20030812
DK 2003-1646	A	20031105
US 2003-519212P	P	20031112

AB Title conjugate used as medicament comprising a mono disperse branched polymer covalently attached to a peptide, such as growth factor and aprotinin, is prepared by grafting a monomer, A-L1-X-L2-B' (B' = protected B), to a solid support, such as functionized polystyrene, deprotecting B' to B, coupling a suitable A'-L1-X-L2'-B' (A' = optionally activated form of A), and repeating the last two steps. Thus, 2-(1,3-bis[azidoethoxyethyl]propan-2-yloxy) acetic acid prepared from 2-(2-chloroethoxy)ethanol, epibromohydrin, p-nitrophenylchloroformiate, trichloroacetylchloride, and bromoacetic acid was reacted with 3-hydroxy-1,2,3-benzotrian-4-(3H)-one, reaction product of piperidine and functionalized polystyrene, capped with acetic anhydride, deprotected with dithiothreitol and benzoylchloride, and capped with 2-[2-(2-methoxyethoxy)ethoxy]acetic acid.

IT **11096-26-7DP, EPO**, conjugate with branched polymers
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of branched polymer-peptide conjugates)

L14 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:220384 CAPLUS
DOCUMENT NUMBER: 140:271415
TITLE: Water-soluble polymer alkanals
INVENTOR(S): Kozlowski, Antoni
PATENT ASSIGNEE(S): Nektar Therapeutics Al, Corporation, USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004022630	A2	20040318	WO 2003-US28221	20030909
WO 2004022630	A3	20040415		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2498167	AA	20040318	CA 2003-2498167	20030909
US 2004116649	A1	20040617	US 2003-659734	20030909
EP 1546235	A2	20050629	EP 2003-752147	20030909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003014172	A	20050726	BR 2003-14172	20030909
EP 1591467	A1	20051102	EP 2005-76371	20030909
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, BA, HR, IS, YU				
NO 2005001077	A	20050408	NO 2005-1077	20050228
NO 2005001078	A	20050408	NO 2005-1078	20050228
PRIORITY APPLN. INFO.:			US 2002-409251P P	20020909
			US 2003-456580P P	20030319
			US 2003-456850P P	20030321
			EP 2003-752147 A3	20030909
			WO 2003-US28221 W	20030909

AB The present invention is directed to alkanal derivs. of water-soluble polymers such as poly(ethylene glycol), their corresponding **hydrates** and acetals, and to methods for preparing and using such polymer alkanals. The polymer alkanals of the invention are prepared in high purity and exhibit storage stability. Thus, 2.0 g polyethylene glycol Me ether and 0.5 g 4-chlorobutyraldehyde di-Et acetal were reacted in the presence of 4.0 mL 1.0 M potassium tert-butoxide tert-butanol solution at 100-105° to give 1.6 g methoxy polyethylene glycol butyraldehyde di-Et acetal, 1.0 g of which was hydrolyzed to give 0.72 g methoxy polyethylene glycol butyraldehyde, which was used for pegylation of lysozyme.

IT **11096-26-7DP, EPO**, reaction products with methoxy polyoxyalkylene butyral
RL: IMF (Industrial manufacture); PREP (Preparation)
(preparation of water-soluble polymer alkanals for pegylation of lysozyme)

L14 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1962:471984 CAPLUS
DOCUMENT NUMBER: 57:71984
ORIGINAL REFERENCE NO.: 57:14339f-h
TITLE: Iron storage and transport in experimental hemolytic anemia in the albino rat
AUTHOR(S): Morgan, E. H.
CORPORATE SOURCE: Univ. Western Australia, Nedlands
SOURCE: Journal of Pathology and Bacteriology (1962), 84, 65-72
CODEN: JPBAA7; ISSN: 0368-3494
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Acute and chronic hemolytic anemia was produced in rats by administration of phenylhydrazine-HCl or methyl cellulose. The anemia was accompanied by marked increases in liver and spleen storage of Fe, but with little alteration in the distribution of the Fe between ferritin and hemosiderin. The Fe in both storage forms appeared to be readily available when required by the bone marrow for hemoglobin synthesis. An increase in Fe absorption, greater with phenylhydrazine than with methyl cellulose, occurred with both hemolytic agents. The plasma Fe concentration was elevated only during the early stages of acute hemolytic anemia, whereas the plasma

total Fe-binding capacity was increased in both acute and chronic hemolytic anemia; it seems to be closely related to the rate of **erythropoiesis** in both rat and rabbit, but not to tissue storage Fe levels. 20 references.

IT **100-63-0, Hydrazine**, phenyl-
(anemia from, Fe metabolism in)

L14 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1932:15490 CAPLUS
DOCUMENT NUMBER: 26:15490
ORIGINAL REFERENCE NO.: 26:1664b-h
TITLE: The effect of phenylhydrazine and of phenylhydroxylamine on the metabolism of the red blood cells. A method for measuring the red cell metabolism
AUTHOR(S): Warburg, Otto; Kubowitz, Fritz; Christian, Walter
SOURCE: Biochemische Zeitschrift (1931), 242, 170-205
CODEN: BIZEA2; ISSN: 0366-0753
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB cf. C. A. 25, 4033. Methemoglobin, produced in blood cells by means of Am nitrite, oxidizes carbohydrate with the formation of hemoglobin as the reduction product which is changed to oxyhemoglobin on shaking the cells with O. The cells which were made brown by the Am nitrite again become bright red. The methemoglobin reacts stoichiometrically and not as a catalyst, each reduced atom of Fe remaining so and the O uptake having come to an end when the methemoglobin has been changed back to oxyhemoglobin. The methemoglobin produced in the red cells by means of phenylhydroxylamine behaves quite differently. Anaerobically the methemoglobin is reduced by carbohydrate to hemoglobin, and when the reduction is completed saturation with air causes a change of the brown color to bright red because of the formation of oxyhemoglobin. But when the methemoglobin and carbohydrate react in the red cells in the presence of O, methemoglobin is formed instead of oxyhemoglobin on the reoxidation of the Fe, and the cells retain their brown color while they consume O. Here the Fe acts catalytically, and a given amount of methemoglobin can serve to transmit any quantity of O. The "phenylhydroxylamine respiration" of the rabbit red blood cell is about 20 times as great as the normal. Phenylbydrazine added to the red blood cells in vitro also colors them brown and greatly promotes their respiration. Phenylhydrazine decomposes the hemoglobin into free hemin and denatured globin. Shaking such cells with air causes oxidation of carbohydrate with the formation of CO2, and the O consumption of the cells increases 10- 20 times. The color remains brown although the cells still contain oxyhemoglobin. The Fe catalysis in this instance is more complicated, the free hemin oxidizing oxyhemoglobin to methemoglobin and the methemoglobin oxidizing the carbohydrate. Haem is now reoxidized by O to hemin, and hemoglobin combines with O to oxyhemoglobin, thus re.acte.establishing the original condition. In this case an autoxidizable Fe of haem and a non-autoxidizable Fe of hemoglobin co.acte.operate in this catalysis. The findings of Morowitz that the respiration of the red blood cells from rabbits injected with phenylhydrazine is increased 20-40 times is corroborated, and this is apparently due to the greater number of young erythrocytes inasmuch as phenylhydrazine stimulates **erythropoiesis**. But the cells in Morowitz' expts. are not brown as is the case in the in vitro expts; they do not contain any demonstrable amts. of free hemin but denatured globin. The phenylhydrazine affects the young erythrocytes which somehow rid themselves of the free hemin. The difference between the in vitro and in vivo expts. is this, that whereas in the former O is transmitted by large amts. of blood heroin, in the latter the transfer is due to immeasurably small quantities of enzyme heroin, and this can be inhibited by traces of HCN or by CO (light reversible).

IT **100-63-0, Hydrazine**, phenyl-
(effect on metabolism of red blood cells)

L14 ANSWER 37 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:394682 CAPLUS
DOCUMENT NUMBER: 142:445550
TITLE: Gene expression profiles for the diagnosis and prognosis of breast cancer

INVENTOR(S): Erlander, Mark; Ma, Xiao-Jun; Wang, Wei; Wittliff, James L.
PATENT ASSIGNEE(S): Arcturus Bioscience, Inc. University of Louisville, USA
SOURCE: U.S. Pat. Appl. Publ., 40 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005095607	A1	20050505	US 2004-795092	20040305
WO 2005098037	A1	20051020	WO 2004-US6760	20040305

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-453006P P 20030307

AB The invention relates to the identification and use of gene expression profiles, or patterns, suitable for identification of breast cancer patient populations with different survival outcomes. The gene expression profiles may be embodied in nucleic acid expression, protein expression, or other expression formats, and may be used in the study and/or determination of the prognosis of a patient, including breast cancer survival.

IT **127464-60-2**, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); BIOL (Biological study); USES (Uses)
(gene for, in breast cancer diagnosis; gene expression profiles for diagnosis and prognosis of breast cancer)

L14 ANSWER 38 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:1997 CAPLUS
DOCUMENT NUMBER: 142:111841
TITLE: Gene expression profiles and biomarkers for the detection of depression-related and other disease-related gene transcripts in blood
INVENTOR(S): Liew, Choong-Chin
PATENT ASSIGNEE(S): Chondrogene Limited, Can.
SOURCE: U.S. Pat. Appl. Publ., 154 pp., Cont.-in-part of U.S. Ser. No. 802,875.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 47
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004265868	A1	20041230	US 2004-812702	20040330
US 2004014059	A1	20040122	US 2002-268730	20021009
US 2005191637	A1	20050901	US 2004-803737	20040318
US 2005196762	A1	20050908	US 2004-803759	20040318
US 2005196763	A1	20050908	US 2004-803857	20040318
US 2005196764	A1	20050908	US 2004-803858	20040318
US 2005208505	A1	20050922	US 2004-803648	20040318
US 2004265869	A1	20041230	US 2004-812716	20040330
US 2004265868	A1	20041230	US 2004-812702	20040330
US 2004265868	A1	20041230	US 2004-812702	20040330

PRIORITY APPLN. INFO.: US 1999-115125P P 19990106
US 2000-477148 B1 20000104

US 2002-268730	A2	20021009
US 2003-601518	A2	20030620
US 2004-802875	A2	20040312
US 2004-812702	A	20040330

AB The present invention is directed to detection and measurement of gene transcripts and their equivalent nucleic acid products in blood. Specifically provided is anal. performed on a drop of blood for detecting, diagnosing, and monitoring diseases, and in particular mental depression, using gene-specific and/or tissue-specific primers. Affymetrix Human Genome U133 and ChondroChip microarrays were used to detect differentially expressed gene transcripts in hypertension, obesity, allergy, systemic steroids, coronary artery disease, diabetes type 2, hyperlipidemia, lung disease, bladder cancer, rheumatoid arthritis, osteoarthritis, liver cancer, schizophrenia, Chagas disease, asthma, and manic depression syndrome. The present invention describes methods by which delineation of the sequence and/or quantitation of the expression levels of disease-specific genes allows for an immediate and accurate diagnostic/prognostic test for disease or to assess the effect of a particular treatment regimen.

IT **127464-60-2**, Vascular endothelial growth factor
RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(gene expression profiles and biomarkers for the detection of depression-related and other disease-related gene transcripts in blood)

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L14 ANSWER 1 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:184851 CAPLUS
DOCUMENT NUMBER: 136:268102
TITLE: Branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**
INVENTOR(S): Kochendoerfer, Gerd; Botti, Paolo; Bradburne, James A.; Chen, Shiah-Yun; Cressman, Sonya; Hunter, Christie L.; Kent, Stephen B. H.; Low, Donald W.
PATENT ASSIGNEE(S): Gryphon Sciences, USA; Gryphon Therapeutics, Inc.
SOURCE: PCT Int. Appl., 191 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002019963	A2	20020314	WO 2001-US21928	20010712
WO 2002019963	A3	20030206		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2412277	AA	20020314	CA 2001-2412277	20010712
AU 2001078905	A5	20020322	AU 2001-78905	20010712
EP 1315511	A2	20030604	EP 2001-957133	20010712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004515471	T2	20040527	JP 2002-524448	20010712
BR 2001013623	A	20040622	BR 2001-13623	20010712
EE 200300089	A	20050215	EE 2003-89	20010712
US 2003191291	A1	20031009	US 2003-332696	20030113
BG 107590	A	20031231	BG 2003-107590	20030226
NO 2003001049	A	20030508	NO 2003-1049	20030306

PRIORITY APPLN. INFO.:

US 2000-231339P	P	20000908
US 2000-236377P	P	20000929
WO 2001-US21928	W	20010712

AB The invention provides seven synthetic **erythropoiesis** stimulating proteins having one or more branched water-soluble polymers attached thereto, which are analogs of human erythropoietin. The invention also provides methods for the manufacture of the synthetic **erythropoiesis** stimulating proteins by chemical ligating peptide segments comprising non-overlapping amino acid sequences of a polypeptide chain of a synthetic **erythropoiesis** stimulating protein. The invention further relates to derivs. of such synthetic **erythropoiesis** stimulating proteins that are polymer-modified in a defined manner. Methods and uses for such proteins and derivatized proteins are also provided.

IT Proteins
RL: BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(SEP-0; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SEP-1-B50; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SEP-1-B51; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SEP-1-B52; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SEP-1-L26; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SEP-1-L30; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Proteins
RL: BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(SEP-1; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Proteins
RL: BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(SEP-3; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Buffers
Detergents
Preservatives
(as excipient; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Amino acids, biological studies
Lipids, biological studies
Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as excipient; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Human
Mammalia
Oximation
Protein sequences
(branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Polymers, biological studies
RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(branched; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses

thereof for **erythropoiesis**)

IT Amide group
(chemical ligation; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT **Hydrazones**
Oximes
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chemical ligation; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Polyoxyalkylenes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(derivs., water soluble polymer comprising; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**erythropoiesis** stimulating; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Protein motifs
(glycosylation site, water soluble polymer attached to; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Erythrocyte
Reticulocyte
(increasing production of; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Hemoglobins
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(increasing production of; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Drug delivery systems
(liqs., dispersions, mono-; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Erythrocyte
(polycythemia, treatment of; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Drug delivery systems
(polymer-bound; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Glycoproteins
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ribosomal-specific erythropoietin; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT **Erythropoiesis**
(stimulating; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Functional groups
(thio ester group, chemical ligation; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Hypoxia
(treatment of; branched water-soluble polymer-modified synthetic

erythropoiesis stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT Polymers, biological studies
RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(water-soluble; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT 404868-31-1P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(amino acid sequence; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT 404868-32-2P 404868-33-3P 404868-34-4P 404868-50-4P 404868-51-5P 404868-54-8P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT 504-76-7, Oxazolidine 504-78-9, Thiazolidine
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chemical ligation; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT 56-86-0, L-Glutamic acid, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pseudo-, synthetic **erythropoiesis** stimulating protein comprising; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT **11096-26-7**, Erythropoietin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ribosomally specific; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT 404562-11-4 404562-12-5 404562-13-6
RL: PRP (Properties)
(unclaimed protein sequence; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT 75-21-8, Ethylene oxide, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(water soluble polymer comprising; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

IT **11096-26-7**, Erythropoietin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ribosomally specific; branched water-soluble polymer-modified synthetic **erythropoiesis** stimulating proteins and therapeutic uses thereof for **erythropoiesis**)

L14 ANSWER 2 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1963:463892 CAPLUS
DOCUMENT NUMBER: 59:63892
ORIGINAL REFERENCE NO.: 59:11854b-c
TITLE: Sustained high levels of **erythropoiesis** -stimulating factor (**ESF**) in plasma of irradiated phenylhydrazine-treated rats
AUTHOR(S): Eskuche, Irma; Hodgson, G.
CORPORATE SOURCE: Univ. Chile, Santiago
SOURCE: Acta Physiologica Latinoamericana (1962), 12, 282-90
CODEN: APLTAF; ISSN: 0001-6764

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Rats were irradiated with γ-rays (550 r.) from radio cesium, then treated with phenylhydrazine. They became severely anemic and remained so for up to 2 weeks. During this time plasma **ESF** levels were higher than 16 Co units/ml. Rats pretreated with phenylhydrazine and then irradiated became less anemic and showed lower **ESF** levels. Plasma of rats treated only with phenylhydrazine had the same **ESF** levels, for a similar degree of anemia, as the irradiated, phenylhydrazine-treated rats. Only rats with <7 g. hemoglobin/100 ml. of blood showed appreciable **ESF** activity in plasma and the **ESF** activity increased exponentially with the severity of anemia (quant. data given).
IT Gamma rays
(erythropoietin in blood plasma after phenylhydrazine and)
IT Blood plasma
(erythropoietins in, γ-ray effect on, phenylhydrazine in relation to)
IT **100-63-0**, **Hydrazine**, phenyl-
(erythropoietins in blood plasma after γ-irradiation and)
IT **11096-26-7**, Erythropoietin
(in blood plasma, after γ-irradiation, phenylhydrazine and)
IT **100-63-0**, **Hydrazine**, phenyl-
(erythropoietins in blood plasma after γ-irradiation and)
IT **11096-26-7**, Erythropoietin
(in blood plasma, after γ-irradiation, phenylhydrazine and)

L14 ANSWER 3 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:471022 CAPLUS
DOCUMENT NUMBER: 122:236269
TITLE: Inhibition of heme synthesis induces apoptosis in human **erythroid** progenitor cells
AUTHOR(S): Muta, Koichiro; Krantz, Sanford B.
CORPORATE SOURCE: Dep. Medicine, Department of Veterans Affairs Medical Center, Nashville, TN, 37232, USA
SOURCE: Journal of Cellular Physiology (1995), 163(1), 38-50
CODEN: JCLLAX; ISSN: 0021-9541
PUBLISHER: Wiley-Liss
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Heme synthesis by **erythroid** progenitor cells is maintained by erythropoietin (EP), insulin-like growth factor-I (IGF-I), and stem cell factor (SCF), and without these growth factors apoptosis (programmed cell death) occurs. To clarify the possible interaction between heme synthesis and programmed cell death of human **erythroid** progenitor cells, the effect of specific inhibition of hemes synthesis on apoptosis of highly purified human **erythroid** colony forming cells (ECFC) was studied. When the amount of uncleaved DNA was determined as a measure of apoptosis, the heme synthesis inhibitors, succinylacetone (SA) (0.1 mmol/L) or isonicotinic acid **hydrazide** (INH) (10 mmol/L), significantly decreased the amount of uncleaved DNA ($P < 0.01$) in the presence of erythropoietin (EP). Addition of recombinant heavy-chain ferritin (rHF) (10 nmol/L), or deprivation of transferrin from the culture medium, which decreased heme synthesis, also reduced the amount of uncleaved DNA ($P < 0.01$). The production of apoptosis by diverse inhibitors of heme synthesis was in each case reversed by the addition of hemin (0.1 mmol/L) and did not occur with HL-60 cells. When the colony-forming capacity of ECFC was determined by plasma clot assay, SA, INH, or rHF reduced the number of CFU-E ($P < 0.01$), and the effect of SA was reversed by hemin. The addition of SA did not alter the c-myc response of ECFC to EP. These data indicate that inhibition of heme synthesis induces apoptosis of human **erythroid** progenitor cells, in a manner independent of an early c-myc response, and suggest that the presence of apoptosis in ineffective **erythropoiesis** may be secondary to impaired heme synthesis.
IT Ferritins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(heavy-chain; inhibition of heme synthesis induces apoptosis in human **erythroid** progenitor cells in relation to)

IT Apoptosis
(inhibition of heme synthesis induces apoptosis in human **erythroid** progenitor cells)
IT **Erythropoiesis**
(inhibition of heme synthesis induces apoptosis in human **erythroid** progenitor cells in relation to)
IT Transferrins
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of heme synthesis induces apoptosis in human **erythroid** progenitor cells in relation to)
IT Hematopoietic precursor cell
(**erythroid**, inhibition of heme synthesis induces apoptosis in human **erythroid** progenitor cells)
IT 14875-96-8, Heme
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(inhibition of heme synthesis induces apoptosis in human **erythroid** progenitor cells)
IT **11096-26-7**, Erythropoietin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of heme synthesis induces apoptosis in human **erythroid** progenitor cells in relation to)
IT **11096-26-7**, Erythropoietin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(inhibition of heme synthesis induces apoptosis in human **erythroid** progenitor cells in relation to)

L14 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1973:119294 CAPLUS
DOCUMENT NUMBER: 78:119294
TITLE: Changes in marrow hemopoiesis in rats with sarcoma M-1 treated with β-(5-nitro-2-furyl)acrolein N,N-bis(2-chloroethyl)**hydrazone** (IF-202) and B-group vitamins
AUTHOR(S): Prane, L.
CORPORATE SOURCE: Latv. Nauchno-Issled. Inst. Eksp. Klin. Med., Riga, USSR
SOURCE: Protivoopukholevye Soedin. 5-Nitrofuranovogo Ryada (1972), 197-208. Editor(s): Giller, S. A. "Zinatne": Riga, USSR.
CODEN: 26FJAO
DOCUMENT TYPE: Conference
LANGUAGE: Russian
AB β-(5-Nitro-2-furyl)acrolein n,N-bis(2-chloroethyl) **hydrazone** (I) [19819-47-7] (25 mg/kg, s.c.) injected daily for 10 days into rats with M-1 sarcoma decreased myelopoiesis by decreasing the total number of myeloid cells at the expense of immature and young cells. The I treatment also disrupted the maturation of neutrophils and, to a lesser degree, that of **erythroid** components, and increased the degeneration of formed elements which was already visible during tumor development. The suppression of bone marrow blood formation by I was somewhat greater at 10 days after the last injection than during the injections. The oral administration of B vitamins (thiamine [59-43-8] and pyridoxal [**66-72-8**], 1mg/kg each; riboflavine [83-88-5], 0.4 mg/kg; nicotinic acid [59-67-6] and pantothenic acid [79-83-4], 1.8 mg/kg each; inositol [87-89-8] and folic acid [59-30-3], 0.08 mg/kg each; choline chloride [67-48-1], 20mg/kg) during treatment with I decreased the toxic effect of I on the bone marrow and decreased the inhibition of leukopoiesis, both immediately after the treatment and at 10 days thereafter.
IT Hemopoiesis
(acrolein **hydrazone** derivative inhibition of, vitamin B effect on, in neoplasm)
IT Neoplasm-host relationship
(hemopoiesis in, acrolein **hydrazone** derivative and vitamin B effect on)

IT 59-30-3, biological studies 59-43-8, biological studies 59-67-6, biological studies **66-72-8** 67-48-1 79-83-4 83-88-5, biological studies 87-89-8
RL: BIOL (Biological study)
(hemopoiesis inhibition by acrolein **hydrazones** derivative response to, in neoplasm)
IT 19819-47-7
RL: BIOL (Biological study)
(hemopoiesis inhibition by, vitamin B effect on, in neoplasm)
IT **66-72-8**
RL: BIOL (Biological study)
(hemopoiesis inhibition by acrolein **hydrazones** derivative response to, in neoplasm)

L14 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:89200 CAPLUS
DOCUMENT NUMBER: 139:4888
TITLE: Austrian Moderate Altitude Study (AMAS 2000) - fluid shifts, **erythropoiesis**, and angiogenesis in patients with metabolic syndrome at moderate altitude (.simeq.1700 m)
AUTHOR(S): Gunga, Hanns-Christian; Fries, Dietmar; Humpeler, Egon; Kirsch, Karl; Boldt, Leif-Erik; Koralewski, Eberhard; Johannes, Bernd; Klingler, Anton; Mittermayr, Markus; Roecker, Lothar; Yaban, Berrin; Behn, Claus; Jelkmann, Wolfgang; Schobersberger, Wolfgang
CORPORATE SOURCE: Universitaetsklinikum Benjamin Franklin, Institut fuer Physiologie, Zentrum fuer Weltraummedizin Berlin (ZWMB), Freie Universitaet Berlin, Berlin, 14195, Germany
SOURCE: European Journal of Applied Physiology (2003), 88(6), 497-505
CODEN: EJAPFN; ISSN: 1439-6319
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It was hypothesized that subjects with metabolic syndrome (hypertension, obesity, hyperlipidemia, diabetes mellitus): (1) develop measurable peripheral edema at moderate altitude and (2) might show differences on **erythropoiesis**, iron status and vascular endothelial growth factor (VEGF) in comparison to healthy subjects during and after a long-term stay (3-wk exposure) at moderate altitude (.simeq.1700 m). Twenty-two male subjects with metabolic syndrome were selected. Baseline investigations (t1) were performed in Innsbruck (500 m). All participants were transferred by bus to 1700 m (Alps) and remained there for 3 wk with examns. on day 1 (after the first night at altitude, t2), day 4 (t3), day 9 (t4) and day 19 (t5). After returning to Innsbruck, post-altitude examns. were conducted after 7-10 days (t6) and 6-7 wk (t7), resp. Body mass was decreased from t1 to t7 ($P<0.01$). Total body water was decreased at t2 ($P<0.01$), returned to control level (t3, t4), and was found elevated at t7 ($P<0.01$). Lean body mass did not change, but body fat decreased during the study ($P<0.01$). Tissue thickness at the forehead decreased during and after altitude exposure ($P<0.01$), whereas tissue thickness at the tibia did not alter. Erythropoietin (**EPO**) was elevated as early as t2 and remained increased until t5. Reticulocyte count was increased at t3 and remained above pre-altitude values. VEGF levels were unchanged. After a 3-wk exposure to moderate altitude, patients with metabolic syndrome had reduced their body mass, mainly because of a reduction in body fat. The moderate altitude was found to stimulate **erythropoiesis** in these patients but this was not sufficient to increase serum VEGF concentration
IT Adipose tissue
Angiogenesis
Erythropoiesis
Human
Hydration, physiological
Reticulocyte
(fluid shifts, **erythropoiesis**, and angiogenesis in patients

with metabolic syndrome at moderate altitude (.simeq.1700 m))
IT Transferrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fluid shifts, **erythropoiesis**, and angiogenesis in patients with metabolic syndrome at moderate altitude (.simeq.1700 m))
IT Atmosphere (environmental)
(high-altitude; fluid shifts, **erythropoiesis**, and angiogenesis in patients with metabolic syndrome at moderate altitude (.simeq.1700 m))
IT Disease, animal
(metabolic syndrome X; fluid shifts, **erythropoiesis**, and angiogenesis in patients with metabolic syndrome at moderate altitude (.simeq.1700 m))
IT 7439-89-6, Iron, biological studies **11096-26-7**, Erythropoietin **127464-60-2**, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fluid shifts, **erythropoiesis**, and angiogenesis in patients with metabolic syndrome at moderate altitude (.simeq.1700 m))
IT **11096-26-7**, Erythropoietin **127464-60-2**, Vascular endothelial growth factor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fluid shifts, **erythropoiesis**, and angiogenesis in patients with metabolic syndrome at moderate altitude (.simeq.1700 m))
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:995718 CAPLUS
DOCUMENT NUMBER: 141:416010
TITLE: Erythropoietin conjugate compounds with extended half-lives
INVENTOR(S): Heavner, George
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004229318	A1	20041118	US 2003-439870	20030517
WO 2004106373	A1	20041209	WO 2003-US15750	20030520

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR

PRIORITY APPLN. INFO.: US 2003-439870 A 20030517
AB The invention provides biol. active erythropoietin (**EPO**) conjugate compns. wherein **EPO** is covalently conjugated to a non-antigenic hydrophilic polymer covalently linked to an organic mol. that increases the circulating serum half-life of the composition The invention thus relates to **EPO** derivs. described by the formula **EPO** -(X-Y) N where **EPO** is erythropoietin or its pharmaceutically acceptable derivs. having biol. properties of causing bone marrow cells to increase production of reticulocytes and red blood cells, X is PEG or other water soluble polymers, Y is an organic mol. that increases the circulating half-life of the construct more than the PEG alone and N is an integer from 1 to 15. Other mols. may be included between **EPO** and X and between X and Y to provide the proper functionality for coupling or valency. For example, erythropoietin was conjugated to DSPE-PEG through the alpha amino group of amino acid 1 of erythropoietin, and was able to prolong the serum half-life of erythropoietin in mice shown by the high

hematocrit and Hb levels.

IT Anemia (disease)
Bone marrow
Erythrocyte
(erythropoietin conjugates with polymers and orgs. for extended serum half-lives)

IT Amino acids, biological studies
Carbohydrates, biological studies
Fatty acids, biological studies
Lipids, biological studies
Phospholipids, biological studies
Polyoxyalkylenes, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(erythropoietin conjugates; erythropoietin conjugates with polymers and orgs. for extended serum half-lives)

IT Fatty acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(esters, erythropoietin conjugates; erythropoietin conjugates with polymers and orgs. for extended serum half-lives)

IT 76-05-1, Trifluoroacetic acid, uses 7087-68-5, Diisopropylethylamine
RL: NUU (Other use, unclassified); USES (Uses)
(erythropoietin conjugates with polymers and orgs. for extended serum half-lives)

IT **11096-26-7DP**, Erythropoietin, derivs., conjugates with PEG-DSPE/PEG-linoleate 145035-96-7DP, conjugates with erythropoietin, lysylglycyl peptides
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(erythropoietin conjugates with polymers and orgs. for extended serum half-lives)

IT 530-62-1, 1,1'-Carbonyldiimidazole **11096-26-7**, Erythropoietin 145035-96-7D, PEG-DSPE, NHS ester 171550-47-3D, NHS ester, conjugates with erythropoietin 198227-38-2 792987-32-7 792987-34-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(erythropoietin conjugates with polymers and orgs. for extended serum half-lives)

IT 792987-34-9DP, PEG derivs.
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(erythropoietin conjugates with polymers and orgs. for extended serum half-lives)

IT 598-21-0, Bromoacetyl bromide
RL: RGT (Reagent); RACT (Reactant or reagent)
(erythropoietin conjugates with polymers and orgs. for extended serum half-lives)

IT 792987-33-8DP, conjugates with PEG and erythropoietin
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(erythropoietin conjugates with polymers and orgs. for extended serum half-lives)

IT 302-01-2D, **Hydrazine**, PEG and erythropoietin conjugates
629-80-1D, Palmitaldehyde, erythropoietin conjugates 4537-76-2D, Distearoyl phosphatidyl ethanolamine, erythropoietin conjugates
9003-39-8D, Polyvinyl pyrrolidone, erythropoietin conjugates
25322-68-3D, PEG, substitutes, erythropoietin conjugates 25322-69-4D, Polypropylene glycol, erythropoietin conjugates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(erythropoietin conjugates with polymers and orgs. for extended serum half-lives)

IT **11096-26-7DP**, Erythropoietin, derivs., conjugates with PEG-DSPE/PEG-linoleate
RL: PKT (Pharmacokinetics); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(erythropoietin conjugates with polymers and orgs. for extended serum half-lives)

IT **11096-26-7**, Erythropoietin
RL: RCT (Reactant); RACT (Reactant or reagent)
(erythropoietin conjugates with polymers and orgs. for extended serum half-lives)

L14 ANSWER 7 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1950:23178 CAPLUS
DOCUMENT NUMBER: 44:23178
ORIGINAL REFERENCE NO.: 44:4589h-i
TITLE: Effect of synthetic antithyroid compounds on **erythropoiesis** in experimental phenylhydrazine-induced anemia
AUTHOR(S): Telo, Walter
CORPORATE SOURCE: Univ. Parma, Italy
SOURCE: Giorn. clin. med. (1949), 30, 113-26
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Reticulosis induced in guinea pigs with phenylhydrazine is prevented by the administration of 0.3 to 1 g./day of 4-methylthiouracil (I) or 60 to 200 mg./day of 5,5-diethyl-2-thiobarbituric acid (II) for 15 to 40 days. The duration of the treatment rather than the amount of compound dets. the amount of inhibition. I is somewhat more effective than II.
IT Anemia
(from phenylhydrazine, antithyroid compound effect on **erythropoiesis** in)
IT **Erythropoiesis**
(in phenylhydrazine anemia, effect of antithyroid compds. on)
IT **100-63-0**, **Hydrazine**, phenyl-
(anemia from, effect of antithyroid compds. on **erythropoiesis** in)
IT 56-04-2, Uracil, 6-methyl-2-thio- 77-32-7, Barbituric acid, 5,5-diethyl-2-thio-
(effect on **erythropoiesis** in phenylhydrazine anemia)
IT **100-63-0**, **Hydrazine**, phenyl-
(anemia from, effect of antithyroid compds. on **erythropoiesis** in)

L14 ANSWER 8 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:540453 CAPLUS
DOCUMENT NUMBER: 143:53491
TITLE: Methods and compositions using immunomodulatory compounds for the treatment and management of hemoglobinopathy and anemia
INVENTOR(S): Moutouh-de Parseval, Laure; Chan, Kyle W. H.; Brady, Helen
PATENT ASSIGNEE(S): Celgene Corporation, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005055929	A2	20050623	WO 2004-US40226	20041202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2005143420	A1	20050630	US 2004-4736	20041202
PRIORITY APPLN. INFO.:			US 2003-526910P P	20031202

OTHER SOURCE(S): MARPAT 143:53491
AB The present invention is directed to the use of immunomodulatory compds., particularly members of the class of compds. known as IMiDsTM, and more specifically the compds. 4-(Amino)-2-(2,6-dioxo(3-piperidyl))-isoindoline-

1,3-dione and 3-(4-amino-1-oxo-1,3-dihydroisoindol-2-yl)-piperidine-2,6-dione, to induce the expression of fetal Hb genes, genes essential for **erythropoiesis**, and genes encoding alpha Hb stabilizing protein, within a population of CD34+ cells. These compds. are used to treat hemoglobinopathies such as sickle cell anemia or β-thalassemia, or anemias caused by disease, surgery, accident, or the introduction or ingestion of toxins, poisons or drugs. CD34+ progenitor cells were first expanded with a combination of growth factors (stem cell factor (SCF), Flt3-L and IL-3) for 6 days, and **erythroid** differentiation was then induced with SCF and **Epo** for 6 days. During the **erythroid** differentiation period CD34+ cells were cultured in the presence or absence of IMiD 4-(Amino)-2-(2,6-dioxo(3-piperidyl))isoindoline-1,3-dione, alone or in combination with either hydroxyurea and 5-azacytidine, in order to compare the effect of IMiDs to these two known inducers of fetal Hb synthesis. On day 6 of differentiation, the Hb content of the cells was measured by flow cytometry. Interestingly, 4-(Amino)-2-(2,6-dioxo(3-piperidyl))isoindoline-1,3-dione showed a striking synergy in combination with hydroxyurea, resulting in a striking reactivation of fetal Hb.

IT Glycophorins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(A; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(AHSP (α Hb stabilizing protein), induction of expression of gene for; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Bone marrow
(CD34-pos. hematopoietic progenitor cells derived from, differentiation to dendritic cells with upregulated **erythroid**-specific genes; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Stem cell
(CD34-pos., modulation of differentiation of, to **erythroid** lineage; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(EKLF (**erythroid** Kruppel-like factor); immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Hemopoietins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FLT3 ligand, as addnl. agent; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Potassium channel blockers
(Gardos channel antagonist, as addnl. agent; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Blood-group substances
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(K (Kell), precursor; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(STAT5 (signal transducer and activator of transcription 5), phosphorylation of; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Erythrocyte
(adhesion, compound reducing, as addnl. agent; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Accident
Chemotherapy
Disease, animal
Drugs
Poisons, nonbiological source

Surgery
(anemia caused by; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Toxins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(anemia caused by; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Aldehydes, biological studies
Cytokines
Interleukin 3
Stem cell factor
Tumor necrosis factors
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as addnl. agent; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Vasodilators
(as addnl. agents; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Dendritic cell
(bone marrow-derived CD34-pos. hematopoietic progenitor cells differentiation to, with upregulated **erythroid**-specific genes; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT CD34 (antigen)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cells pos. for, induction of genes for fetal Hb and **erythropoiesis** in; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Hematopoietic precursor cell
(**erythroid**, modulation of differentiation of CD34-pos. stem cell to; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Embryophyta
(extract having antisickling activity, as addnl. agent; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Gene, animal
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(for fetal Hb and **erythropoiesis** and α Hb stabilizing protein, induction of expression of; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Glycophorins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(glycophorin B; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Anemia (disease)
Combination chemotherapy
Drug delivery systems
Human
Immunomodulators
Mammalia
Sickle cell anemia
Signal transduction, biological
Thalassemia
(immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Polyoxyalkylenes, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT **Erythropoiesis**
(induction of expression of genes for; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Hemoglobins
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)

(metabolic disorders, hemoglobinopathy; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(monoclonal, as addnl. agent; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Cell differentiation
(of CD34-pos. stem cell to **erythroid** lineage, modulation of; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Adhesion, biological
(of erythrocytes, compound reducing, as addnl. agent; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Solvates
Stereoisomers
(of immunomodulatory compound; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Clathrates
Hydrates
Salts, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of immunomodulatory compound; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Drug delivery systems
(prodrugs, of immunomodulatory compound; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Phosphorylation, biological
(protein, of STAT5; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rhesus blood group associated; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Aggregation
(self-aggregation, of HbS, compound reducing, as addnl. agent; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Drug interactions
(synergistic; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT Thalassemia
(β-; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT 74-82-8D, Methane, triaryl derivs. 107-92-6, Butanoic acid, biological studies 107-92-6D, Butanoic acid, derivs. 113-00-8D, Guanidine, derivs. 127-07-1, Hydroxyurea 10024-97-2, Nitrous oxide, biological studies **11096-26-7**, Erythropoietin 23593-75-1, Clotrimazole 25322-68-3D, Polyethylene glycol, derivs. 83869-56-1, GM-CSF
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as addnl. agent; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT 50-35-1D, Thalidomide, amino-substituted compds. 19171-19-8 19171-19-8D, analogs, prodrugs 191732-70-4 191732-72-6 191732-72-6D, analogs, prodrugs 191732-74-8 191732-76-0
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as immunomodulatory compound; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT 9035-22-7, Hemoglobin S
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(compound reducing self-aggregation of, as addnl. agent; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT 9034-51-9, Hemoglobin A

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT 320-67-2, 5-Azacytidine
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT 9034-63-3, Fetal Hb
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(induction of expression of genes for; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

IT **11096-26-7**, Erythropoietin
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as addnl. agent; immunomodulatory compds. and compns. for treatment and management of hemoglobinopathy and anemia)

L14 ANSWER 9 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:184917 CAPLUS
DOCUMENT NUMBER: 136:268103
TITLE: Method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties
INVENTOR(S): Kochendoerfer, Gerd; Kent, Stephen B. H.; Botti, Paolo; Low, Donald W.; Bradburne, James A.; Chen, Shiah-Yun; Cressman, Sonya; Hunter, Christie L.; Kent, Stephen B. H.; Low, Donald W.; Wilken, Jill G.
PATENT ASSIGNEE(S): Gryphon Sciences, USA
SOURCE: PCT Int. Appl., 245 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002020033	A1	20020314	WO 2001-US21930		20010712
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
CA 2412278	AA	20020314	CA 2001-2412278		20010712
AU 2001073385	A5	20020322	AU 2001-73385		20010712
BR 2001013579	A	20030617	BR 2001-13579		20010712
EP 1318827	A1	20030618	EP 2001-952654		20010712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004508338	T2	20040318	JP 2002-524516		20010712
US 2004115774	A1	20040617	US 2003-332385		20030108
NO 2003001047	A	20030508	NO 2003-1047		20030306
PRIORITY APPLN. INFO.:			US 2000-231339P	P	20000908
			US 2000-236377P	P	20000929
			WO 2001-US21930	W	20010712

AB The present invention relates to methods and compns. for modifying peptides, polypeptides and proteins with polymers, especially glyco-mimetic polymers, so as to improve their biol. activity or pharmacokinetic properties. The invention provides seven synthetic **erythropoiesis** stimulating proteins and four RANTES derivs. having one or more branched water-soluble polymers attached thereto. The invention further provides methods and uses for such polymer-modified peptides, polypeptides and proteins. The invention is particularly suitable for use in the synthesis of polymer-modified synthetic bioactive proteins (Figure 1D), and of pharmaceutical compns. that contain such proteins.

IT Proteins
RL: BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(SEP-0; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SEP-1-B50; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SEP-1-B51; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SEP-1-B52; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SEP-1-L26; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(SEP-1-L30; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Proteins
RL: BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(SEP-1; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Proteins
RL: BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(SEP-3; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Functional groups
(alkoxycarbonyl groups, chemical ligation; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Functional groups
(amino-carboxylate, as branching core; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Amino group
(as branching core; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or

pharmacokinetic properties)
IT Buffers
Detergents
Preservatives
(as excipient; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)
IT Amino acids, biological studies
Lipids, biological studies
Transport proteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as excipient; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)
IT Carboxyl group
Hydroxyl group
(as ionizable group; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)
IT Epoxy group
Formyl group
Sulfhydryl group
(as unique polymer functional group; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)
IT Carboxylic acids, biological studies
Halogens
Ketones, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as unique polymer functional group; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)
IT Polymers, biological studies
RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(branched; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)
IT Amide group
(chemical ligation; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)
IT **Hydrazones**
Oximes
Thioethers
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chemical ligation; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)
IT Polyoxyalkylenes, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(derivs., water soluble polymer comprising; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)
IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**erythropoiesis** stimulating; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)
IT Functional groups
(ether groups, chemical ligation; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)
IT Protein motifs
(glycosylation site, water soluble polymer attached to; method for

modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Erythrocyte
(increasing production of; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Carboxyl group
(ionized, as branching core; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Drug delivery systems
(liqs., dispersions, mono-; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Fusion, biological
Human
Mammalia
Molecular weight
Oximation
Protein sequences
(method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Erythrocyte
(polycythemia, treatment of; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Drug delivery systems
(polymer-bound; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT RANTES (chemokine)
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polymer-modified derivs.; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Chemokines
Cytokines
Glycoproteins
Growth factors, animal
Interferons
Interleukins
Lymphokines
Proteins
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ribosomal-specific; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Hormones, animal, biological studies
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(signal peptide, ribosomal-specific; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT **Erythropoiesis**
(stimulating; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Vinyl compounds, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sulfones, as unique polymer functional group; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Functional groups
(thio ester group, chemical ligation; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol.

activity or pharmacokinetic properties)

IT Hypoxia
(treatment of; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Sulfones
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(vinyl, as unique polymer functional group; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT Polymers, biological studies
RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(water-soluble; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT 404868-31-1P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(amino acid sequence; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT 404868-32-2P 404868-33-3P 404868-34-4P 404868-50-4P 404868-51-5P 404868-54-8P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT 56-84-8, Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 56-87-1, Lysine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as branching core; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT 110-15-6, Succinic acid, biological studies 541-59-3, Maleimide 661-20-1, Isocyanate 1827-97-0 4537-76-2, Distearoyl phosphatidylethanolamine 5681-36-7, Dipalmitoyl phosphatidylethanolamine 7803-62-5, Silane, biological studies 10344-93-1, Acrylate, biological studies 13408-29-2, Aminooxy 14343-69-2, Azide 18358-13-9, Methacrylate, biological studies 23297-32-7, Cyanoacetate 102696-21-9, Succinimidyl succinate 116920-04-8
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(as unique polymer functional group; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT 51-79-6, Urethane 504-76-7, Oxazolidine 504-78-9, Thiazolidine 25415-88-7, **Hydrazide**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(chemical ligation; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT 391198-88-2P, G 1755-01 391198-89-3P, G 1755 404929-17-5P 404929-22-2P
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); PRP (Properties); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT 404928-45-6DP, resin-bound 404928-46-7DP, resin-bound 404928-47-8DP, resin-bound 404928-48-9P 404928-50-3P 404929-05-1P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(method for modifying synthetic proteins with branched water-soluble

polymer to improve their biol. activity or pharmacokinetic properties)

IT 143011-72-7P, Granulocyte colony stimulating factor
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT 62683-29-8P, Colony stimulating factor
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(ribosomal-specific; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT **11096-26-7**, Erythropoietin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ribosomally specific; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT 404882-19-5 404882-20-8 404882-21-9 404882-22-0 404882-23-1
RL: PRP (Properties)
(unclaimed protein sequence; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT 75-21-8, Ethylene oxide, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(water soluble polymer comprising; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

IT **11096-26-7**, Erythropoietin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ribosomally specific; method for modifying synthetic proteins with branched water-soluble polymer to improve their biol. activity or pharmacokinetic properties)

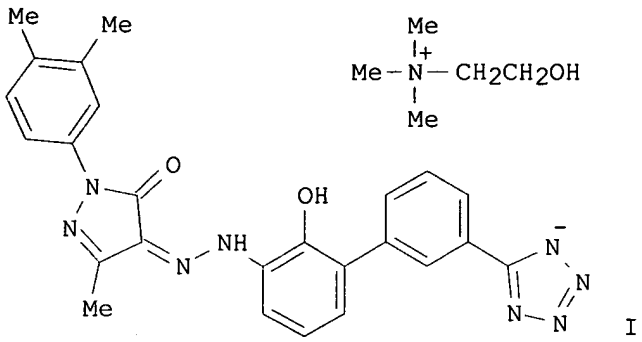
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:405369 CAPLUS
DOCUMENT NUMBER: 142:463730
TITLE: Preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrazol-3-one choline salt
INVENTOR(S): Brook, Christopher S.; Ping, Li-Jen J.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005041867	A2	20050512	WO 2004-US34944	20041021
WO 2005041867	A3	20051013		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-513481P P 20031022
GI



I

AB An improved thrombopoietin mimetic, the choline salt of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrazol-3-one (I), is prepared by treating 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrazol-3-one with choline hydroxide. The compound I is useful as an agonist of thrombopoietin receptor in enhancing platelet production, particularly in the treatment of thrombocytopenia. A tablet and injectable parenteral composition containing I are described.

IT Hemopoietins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(FLT3 ligand, coadministered hematopoietic-cell mobilizing agent; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrazol-3-one choline salt as thrombopoietin receptor agonist)

IT Nervous system, disease
(Huntington's chorea; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrazol-3-one choline salt as thrombopoietin receptor agonist)

IT MPL receptor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(agonist; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrazol-3-one choline salt as thrombopoietin receptor agonist)

IT Nervous system, disease
(amyotrophic lateral sclerosis; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrazol-3-one choline salt as thrombopoietin receptor agonist)

IT Injury
(cerebral, acute brain injury; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrazol-3-one choline salt as thrombopoietin receptor agonist)

IT Ischemia
(cerebral, ischemic brain injury; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrazol-3-one choline salt as thrombopoietin receptor agonist)

IT Chemokines
Cytokines
Interleukin 1
Interleukin 11
Interleukin 3
Interleukin 5
Interleukin 6
Interleukin 8
Interleukins
Leukemia inhibitory factor
Stem cell factor
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministered hematopoietic-cell mobilizing agent; preparation of

2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Blood cell
(cord-blood cells, enhancers for survival and/or proliferation; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Disease, animal
(degenerative; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Nerve, disease
(demyelination; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Platelet (blood)
(disease, thrombocytopenia; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Megakaryocyte
(enhancers for stimulation and/or maturation; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Bone marrow
Stem cell
(enhancers for survival and/or proliferation; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Central nervous system, disease
Nervous system agents
(hereditary myelin disorder; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Heart, disease
(infarction; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Brain, disease
(injury, acute brain injury; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Spinal cord, disease
(injury; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Brain, disease
(ischemia, ischemic brain injury; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Inflammation
Spinal cord, disease
(myelitis, transverse myelitis; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Agranulocytosis
(neutropenia; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Asphyxia
(perinatal asphyxia; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**

]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Blood cell
(peripheral blood stem cells, production enhancers; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Nerve, disease
(peripheral nerve injury; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Injury
(peripheral nerve; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT AIDS (disease)
Alzheimer's disease
Anti-AIDS agents
Anti-Alzheimer's agents
Anti-ischemic agents
Anticonvulsants
Antidiabetic agents
Antiparkinsonian agents
Asphyxia
Cardiovascular agents
Cardiovascular system, disease
Combination chemotherapy
Diabetes mellitus
Digestive tract, disease
Epilepsy
Human
Hypoxia
Kidney, disease
Liver, disease
Multiple sclerosis
Parkinson's disease
(preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Neutrophil
Platelet (blood)
(production enhancers; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Injury
(spinal cord; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Epilepsy
(status epilepticus; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Brain, disease
(stroke; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Blood, disease
(thrombocytopenia; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Head and Neck, disease
(trauma; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT Macrophage inflammatory protein 2
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, coadministered hematopoietic-cell mobilizing agent; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT 9014-42-0, Thrombopoietin **11096-26-7, EPO** 62683-29-8, Colony-stimulating factor 81627-83-0, M-CSF 83869-56-1, GM-CSF 143011-72-7, Granulocyte-colony stimulating factor 209810-58-2, NESP 426847-79-2, Progenipoietin-1 791096-83-8, SD 01
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministered hematopoietic-cell mobilizing agent; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT 851606-62-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT 123-41-1, Choline hydroxide 376592-42-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

IT **11096-26-7, EPO**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministered hematopoietic-cell mobilizing agent; preparation of 2-(3,4-dimethylphenyl)-4-[[2-hydroxy-3'-(1H-tetrazol-5-yl)biphenyl-3-yl]-**hydrazono**]-5-methyl-2,4-dihydropyrozol-3-one choline salt as thrombopoietin receptor agonist)

L14 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:219688 CAPLUS
DOCUMENT NUMBER: 126:259619
TITLE: Effects of erythropoietin on endothelin-1 synthesis and the cellular calcium messenger system in vascular endothelial cells
AUTHOR(S): Vogel, Volker; Kramer, Herbert J.; Baecker, Angela; Meyer-Lehnert, Harald; Jelkmann, Wolfgang; Fandrey, Joachim
CORPORATE SOURCE: Renal Section, Medical Polyclinic and Institute of Physiology I, University of Bonn, Bonn, Germany
SOURCE: American Journal of Hypertension (1997), 10(3), 289-296
CODEN: AJHYE6; ISSN: 0895-7061
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A rise in blood pressure is the main side effect of erythropoietin (**EPO**) treatment in patients with renal anemia. The mechanisms, however, by which **EPO** may cause hypertension are still unclear. We therefore investigated the effects of **EPO** on endothelin (ET) synthesis and cytosolic free calcium concentration ([Ca2+]i) in vascular endothelial cells. Porcine endothelial cells were isolated from thoracic aorta, pulmonary artery, and vena cava. Studies were performed with cells of the first subculture. ET concns. were measured radioimmunol. Changes in [Ca2+]i were determined with the fluorescent probe fura-2. Cytotoxicity was assessed by sodium 3'-[1-(phenyl-amino-carbonyl)-3,4-tetrazolium]-bis(4-methoxy-6-nitro)benzene sulfonic acid **hydrate** (XTT) assay. ET synthesis was similar in cells of different vascular origins and was time-dependent, reaching approx. 2 pmol ET/mg protein within 12 h of incubation. **EPO** (12 to 200 U/mL) stimulated ET release time- and dose-dependently by up to 83.2% within 12 h in the absence of fetal calf serum and heparin. **EPO** induced an immediate significant rise in [Ca2+]i from 58±12 nmol/L to 495±85 nmol/L with a subsequent slow return to 257±3 nmol/L. During 2 h of incubation, the

Ca-ionophore A 23187 (10-8 mol/L) moderately but significantly stimulated endothelial ET synthesis. However, the Ca-channel blocker verapamil, the intracellular Ca-release blocker TMB-8, and nickel, an unspecific calcium channel blocker, had no consistent effects on [Ca2+]i or ET synthesis. The protein kinase C inhibitor H-7 stimulated basal [Ca2+]i and cellular ET synthesis. The tyrosine kinase inhibitor genistein suppressed the **EPO**-induced rise in [Ca2+]i and cellular ET synthesis. From these data we conclude that **EPO** may stimulate ET synthesis in vascular endothelial cells by activation of an **EPO**-receptor and via intracellular signaling mechanisms that comprise tyrosine kinase activation and a rise in [Ca2+]i. Therefore, the systemic hypertensive effects of **EPO** may be due at least in part to local stimulation of vascular endothelial ET synthesis via calcium mobilization.

IT Cytoplasm
(cytosol; erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

IT Blood vessel
(endothelium; erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

IT Biological transport
Hypertension
Second messenger system
Signal transduction, biological
(erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

IT Calcium channel
Erythropoietin receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

IT Dialysis
(hemodialysis; erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

IT Artery
Artery
(pulmonary, endothelium; erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

IT Artery
Artery
(thoracic aorta, endothelium; erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

IT Vein
(vena cava, endothelium; erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

IT **11096-26-7**, Erythropoietin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

IT 7440-70-2, Calcium, biological studies 80449-02-1, Tyrosine kinase 141436-78-4, Protein kinase C
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

IT 123626-67-5, Endothelin-1
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
(erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

IT 7440-70-2, Calcium, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(transport; erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

IT **11096-26-7**, Erythropoietin

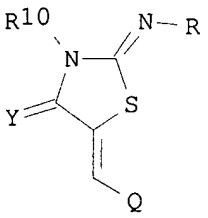
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(erythropoietin effects on endothelin synthesis and cellular calcium messenger system in vascular endothelial cells)

L14 ANSWER 12 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:979651 CAPLUS
DOCUMENT NUMBER: 143:286417
TITLE: Preparation of thiazolone compounds for inhibiting hYAK3 proteins
INVENTOR(S): Duffy, Kevin J.; Fitch, Duke M.; Goodman, Steven Neal; Hasegawa, Masaichi; Johnson, Neil W.; Kasparec, Jiri; Shaw, Antony N.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 162 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005082901	A1	20050909	WO 2005-US6022	20050224

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-547543P P 20040225
OTHER SOURCE(S): MARPAT 143:286417
GI



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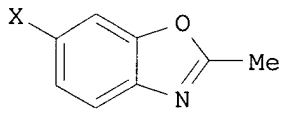

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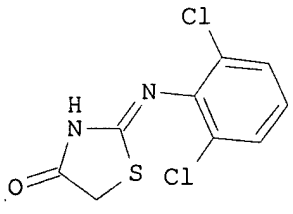
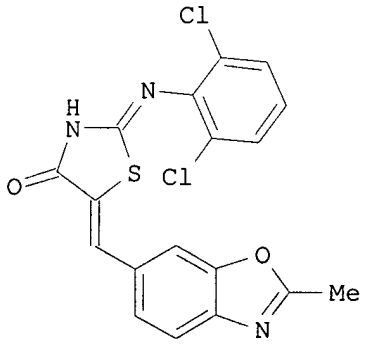


III



IV

AB Title compds. I [wherein R = H, (un)substituted aryl or (cyclo)alkyl; Y = O, S or NR11; R10, R11 = H, alkyl, (CH2)mOH, (CH2)mCOOH; m = 0-6; Q = (un)substituted benzimidazol-6-yl, benzotriazol-6-yl or benzoxazol-6-yl, or pharmaceutically acceptable salts, **hydrates**, solvates or

prodrugs thereof] were prepared for inhibiting hYAK3 proteins. For instance, cyclization of Me 4-amino-3-hydroxybenzoate with tri-Et orthoacetate to II (X = COOMe) (72% yield) followed by reduction with LiAlH4 led to alc. II (X = CH2OH) (58% yield). This compound underwent oxidation with PCC to afford aldehyde II (X = CHO) (66% yield), which was condensed with thiazolidinone III in the presence of piperidine to give IV (15% yield). Compds. IV showed inhibition against hYAK3 kinase enzyme with pIC50 in the range of 8.99-8. Therefore, I and their pharmaceutical compns. (examples given) are useful for treating diseases associated with the imbalance or inappropriate activity of hYAK3 proteins, especially diseases of the **erythroid** and hematopoietic systems.

IT Anemia (disease)
(aplastic, treatment of; preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT Drug delivery systems
(capsules; preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT Blood, disease
(cytopenia, treatment of; preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT Blood cell
(disease, cytopenia, treatment of; preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT Disease, animal
(**erythroid**, treatment of; preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT Drug delivery systems
(parenterals, injectable; preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT Human
(preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT Drug delivery systems
(tablets; preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT Anemia (disease)
Hematopoietic disorders
Myelodysplastic syndromes
Myelosuppression
(treatment of; preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT 471294-42-5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(inhibitor; preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT 864273-75-6P 864273-76-7P 864273-78-9P 864273-82-5P 864273-85-8P
864273-90-5P 864273-94-9P 864273-97-2P 864274-00-0P 864274-01-1P
864274-03-3P 864274-05-5P 864274-06-6P 864274-07-7P 864274-08-8P
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864275-62-7P 864275-63-8P 864275-64-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(inhibitor; preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT 864274-42-0P

RL: BYP (Byproduct); PREP (Preparation)
(preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT 76-05-1, Trifluoroacetic acid, reactions 78-39-7, Triethyl orthoacetate 78-84-2, Isobutyraldehyde 85-41-6, Phthalimide 100-52-7, Benzaldehyde, reactions 108-00-9, N,N-Dimethylethylenediamine 110-91-8, Morpholine, reactions 141-84-4, Rhodanine 500-22-1, 3-Pyridinecarboxaldehyde 590-86-3, Isovaleraldehyde 630-19-3, Pivaldehyde 704-13-2, 3-Hydroxy-4-nitrobenzaldehyde 872-85-5, 4-Pyridinecarboxaldehyde 1003-03-8, Cyclopentylamine 1118-68-9, Dimethylaminoacetic acid **1121-60-4**, 2-Pyridinecarboxaldehyde 2038-03-1, 4-(2-Aminoethyl)morpholine 2516-47-4, Cyclopropylmethylamine 4442-79-9, Cyclohexylethanol 5081-36-7, 3-Methoxy-4-nitrobenzoic acid 5763-55-3, (2-Cyclopentylethyl)amine 6638-79-5, N,O-Dimethylhydroxylamine hydrochloride 15673-00-4, (3,3-Dimethylbutyl)amine 15788-16-6, 1H-Benzimidazole-5-carboxylic acid 20173-24-4, [2-(3-Pyridinyl)ethyl]amine 26386-88-9, DPPA 27578-60-5, 2-Piperidin-1-ylethylamine 34840-23-8 36692-49-6, Methyl 3,4-diaminobenzoate 36743-66-5 62893-54-3, (2-Cyclopropylethyl)amine 63435-16-5, Methyl 4-amino-3-hydroxybenzoate 71605-72-6, 2,1,3-Benzothiadiazole-5-carboxaldehyde 89922-82-7 102191-92-4, 2-[(1,1-Dimethylethyl)dimethylsilyloxy]acetaldehyde 575449-52-4 864274-53-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT 64-04-0P, Benzeneethanamine 98-18-0P 106-47-8P, preparation 109-85-3P 123-00-2P, 4-Morpholinepropanamine 141-43-5P, preparation 462-08-8P, 3-Pyridinamine 1484-85-1P, 1,3-Benzodioxole-5-ethanamine 3182-95-4P 3544-24-9P 5471-55-6P, (2-Cyclohexylethyl)amine hydrochloride 6595-25-1P 13325-10-5P 17823-27-7P 22476-61-5P 26663-77-4P, Methyl 1H-benzimidazole-5-carboxylate 27489-62-9P 35303-76-5P 39130-93-3P 41763-92-2P 58442-17-4P, 1H-Benzimidazole-5-carboxaldehyde 61587-91-5P 64910-48-1P, 3-(Methylamino)-4-nitrobenzonitrile 64910-49-2P, 4-Amino-3-(methylamino)benzonitrile 69570-97-4P 82365-56-8P 90418-06-7P 92241-87-7P 101869-79-8P 106429-29-2P, 1H-Benzimidazole-5-methanol 106429-51-0P 106429-52-1P 114408-87-6P 136663-23-5P 136663-40-6P 174648-21-6P, 2-Phenyl-1H-benzimidazole-5-carboxaldehyde 177476-75-4P 181867-19-6P 214778-10-6P, 3-(Methylamino)-4-nitrobenzoic acid 308362-15-4P 308362-16-5P 308362-19-8P 324578-32-7P 340316-40-7P 425658-25-9P 496846-39-0P 666181-01-7P 701293-60-9P 701294-05-5P 701294-31-7P 828298-25-5P 864273-77-8P 864273-79-0P 864273-80-3P 864273-81-4P 864273-83-6P 864273-84-7P 864273-86-9P 864273-87-0P 864273-88-1P 864273-89-2P 864273-91-6P 864273-92-7P 864273-93-8P 864273-95-0P 864273-96-1P 864273-98-3P 864273-99-4P 864274-02-2P 864274-04-4P 864274-18-0P 864274-19-1P 864274-34-0P 864274-36-2P 864274-37-3P 864274-39-5P 864274-40-8P 864274-41-9P 864274-46-4P 864274-47-5P 864274-50-0P 864274-57-7P 864274-58-8P 864274-59-9P 864274-62-4P 864274-63-5P 864274-64-6P 864274-66-8P 864274-67-9P 864274-69-1P 864274-70-4P 864274-71-5P 864274-72-6P 864274-74-8P 864274-75-9P 864274-76-0P 864274-78-2P 864274-79-3P 864274-81-7P 864274-82-8P 864274-87-3P 864274-88-4P 864274-89-5P 864274-91-9P 864274-92-0P 864274-94-2P 864274-95-3P 864274-96-4P 864274-97-5P 864275-00-3P 864275-01-4P 864275-02-5P 864275-04-7P 864275-05-8P 864275-07-0P 864275-08-1P 864275-10-5P 864275-11-6P 864275-13-8P 864275-14-9P 864275-22-9P 864275-23-0P 864275-65-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of thiazolone compds. for inhibiting hYAK3 proteins)

IT **1121-60-4**, 2-Pyridinecarboxaldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of thiazolone compds. for inhibiting hYAK3 proteins)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 13 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:409226 CAPLUS
DOCUMENT NUMBER: 142:441858
TITLE: Methods of using vitamin D compounds in the treatment of myelodysplastic syndromes

INVENTOR(S): Whitehouse, Martha J.; Curd, John G.
PATENT ASSIGNEE(S): Novacea, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S. Ser. No. 703,140, abandoned.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005101576	A1	20050512	US 2004-841820	20040510
PRIORITY APPLN. INFO.:			US 2003-703140 B2	20031106

AB Methods of treating MDS, or ameliorating a symptom thereof, are disclosed. Specific methods encompass the administration of one or more vitamin D compds., or a pharmaceutically acceptable salt, solvate, **hydrate**, stereoisomer, clathrate, or prodrug thereof, alone or in combination with one or more addnl. active agents. Other methods include intermittent administration of a high dose of one or more vitamin D compds., or a pharmaceutically acceptable salt, solvate, **hydrate**, stereoisomer, clathrate, or prodrug thereof, alone or in combination with one or more addnl. active agents. Such intermittent administration allows high doses of the vitamin D compds. to be administered while minimizing or eliminating hypercalcemia. Patients having low risk MDS and refractory anemia unresponsive to erythropoietin were entered into a Phase 2 trial to evaluate the effect of high dose pulse administration of calcitriol. Patients were administered weekly oral calcitriol at a dose of 45 μg for 20 consecutive weeks. The calcitriol was formulated in a composition containing the following excipients with the amount given in approx. percentage by weight: 65 % MIGLYol 812N, 30 % GELUCIRE 44/14, 5 % vitamin-E TPGS and about 0.05 % each of butylated hydroxytoluene (BHT) and butylated hydroxyanisole (BHA). The high dose pulse administration of calcitriol showed beneficial effect for the treatment of MDS.

IT Glycerides, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C8-10, MIGLYOL 812; vitamin D compds. in treatment of myelodysplastic syndromes)

IT Suspensions
(agent for making, as additive; vitamin D compds. in treatment of myelodysplastic syndromes)

IT Thiols, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antilymphocyte globulins, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)

IT Antibodies and Immunoglobulins
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antithymocyte globulins, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)

IT Antifoaming agents
Antioxidants
Binders
Buffers
Chelating agents
Coloring materials
Fillers
Flavoring materials
Lubricants
Odor and Odorous substances
Opacifiers
Plasticizers
Preservatives

Thickening agents
(as additive; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Cytotoxic agents
Immunomodulators
(as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Cytokines
Growth factors, animal
Hemopoietins
Interleukin 1
Interleukin 11
Interleukin 12
Interleukin 2
Interleukin 3
Interleukin 6
Interleukin 8
Tocopherols
Transcription factors
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Drug delivery systems
(capsules; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Gelatins, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(capsules; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Peptides, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(depsipeptides, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Tackifiers
(detackifiers, as additive; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Signal transduction, biological
(inhibitors, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Drug delivery systems
(injections, i.v.; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Viscosity
(modulators, as additive; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Stability
(of calcitriol capsules; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Solvates
Stereoisomers
(of vitamin D compds.; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Clathrates
Hydrates
Salts, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of vitamin D compds.; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Drug delivery systems
(prodrugs, of vitamin D compds.; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Drug targets
(related to MDS, agents binding to, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)
IT Amines, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(thiol, as addnl. active agent; vitamin D compds. in treatment of

myelodysplastic syndromes)

IT Combination chemotherapy
Human
Myelodysplastic syndromes
(vitamin D compds. in treatment of myelodysplastic syndromes)

IT Interferons
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(α, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)

IT **127464-60-2**, VEGF
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-VEGF, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)

IT 50-02-2, Dexamethasone 50-35-1, Thalidomide 53-03-2, Prednisone 147-94-4, Cytarabine 148-82-3, Melphalan 302-79-4, Retinoic acid 320-67-2, 5-Azacytidine 863-61-6, Menatetrenone 1327-53-3, Arsenic trioxide 1406-18-4D, Vitamin E, derivs. 2353-33-5, Decitabine 4346-18-3, Phenyl butyrate 4759-48-2 6493-05-6, Pentoxifylline 9002-96-4, Vitamin E TPGS 9014-42-0, Thrombopoietin **11096-26-7**, **EPO** 11103-57-4D, Vitamin A, derivs. 12001-79-5D, Vitamin K, derivs. 20537-88-6, Amifostine 20830-81-3, Daunorubicin 21679-14-1, Fludarabine 33419-42-0, Etoposide 58957-92-9, Idarubicin 59865-13-3, Cyclosporin A 65271-80-9, Mitoxantrone 83869-56-1, GM-CSF 123948-87-8, Topotecan 143011-72-7, Granulocyte-colony stimulating factor 185243-69-0, TNFR:Fc 192185-72-1, ZARNESTRA 193275-84-2, SARASAR 204005-46-9, SU5416 212142-18-2 220578-59-6, Gemtuzumab ozogamicin 252916-29-3, SU6668
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)

IT 32222-06-3, Calcitriol
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as vitamin D compound; vitamin D compds. in treatment of myelodysplastic syndromes)

IT 7440-38-2, Arsenic, biological studies
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compound containing, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)

IT 1406-16-2D, Vitamin D, compds.
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vitamin D compds. in treatment of myelodysplastic syndromes)

IT 128-37-0, Butylated hydroxytoluene, biological studies 25013-16-5, Butylated hydroxyanisole 121548-04-7, Gelucire 44/14
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(vitamin D compds. in treatment of myelodysplastic syndromes)

IT **127464-60-2**, VEGF
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(anti-VEGF, as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)

IT **11096-26-7**, **EPO**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(as addnl. active agent; vitamin D compds. in treatment of myelodysplastic syndromes)

L14 ANSWER 14 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1956:83323 CAPLUS
DOCUMENT NUMBER: 50:83323
ORIGINAL REFERENCE NO.: 50:15780g-i,15781a
TITLE: Kinetics of iron metabolism in swine with various experimentally induced anemias
AUTHOR(S): Bush, J. A.; Jensen, W. N.; Ashenbrucker, Helen; Cartwright, G. E.; Wintrobe, M. M.

SOURCE: Journal of Experimental Medicine (1956), 103, 161-71
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB Fe59 was preincubated with plasma from normal pigs and was injected into the ear vein of pigs given PhNHNH2; the mean red-cell survival time was 5 days, the plasma Fe turnover rate was increased about 4-fold, and the rate of **erythropoiesis** was 4- to 5-fold greater than that in the control pigs. In pyridoxine-deficient pigs, the mean red-cell survival time was within normal limits, the plasma Fe turnover rate increased 4-fold, and the rate of **erythropoiesis** was approx. 1/4 the normal mean value. This indicates that a pyridoxine-deficiency anemia is a result of inability of the bone marrow to produce a normal number of red cells. In pteroylglutamic acid-deficient pigs, the mean red-cell survival time was 17 days. The plasma iron turnover rate was 5 times the normal value. The rate of **erythropoiesis** was 1.6 times greater than the mean in control pigs. These data indicate that anemia develops in pteroylglutamic acid deficiency as a result of a combination of a shortening of the red-cell survival time and a limitation of the capacity of the bone marrow to increase red-cell production to the same degree as a normal marrow. The radioactivity in the liver, spleen, and bone marrow of the pteroylglutamic acid-deficient pigs, as determined by measurement of the radioactivity over the body surface, declined more slowly than in control pigs.

IT Isotopes
(as indicators, of Fe metabolism in anemia)
IT **Erythropoiesis**
(in folic acid deficiency and phenylhydrazine anemia)
IT Anemia
(iron metabolism in, in swine)
IT Red blood cells
(iron turnover in, in anemia in swine)
IT Metabolism, animal
(iron, in anemia in swine)
IT **100-63-0**, **Hydrazine**, phenyl-
(anemia from, Fe metabolism in)
IT 8059-24-3, Vitamin B6
(avitaminosis or hypovitaminosis, iron metabolism in anemia in)
IT 59-30-3, Folic acid
(deficiency of, Fe metabolism in)
IT 7439-89-6, Iron
(metabolism of, in Cu deficiency)
IT 7439-89-6, Iron
(metabolism of, in anemia in swine)
IT **100-63-0**, **Hydrazine**, phenyl-
(anemia from, Fe metabolism in)

L14 ANSWER 15 OF 38 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:437103 CAPLUS
DOCUMENT NUMBER: 125:105333
TITLE: Carbohydrate structure of N- and O-linked oligosaccharides of human erythropoietin expressed in Chinese hamster ovary cells
AUTHOR(S): Lee, Dong Eok; Ha, Byung Jhip; Kim, Suk Joon; Park, Ji Sook; Yoo, Ree Ann; Oh, Myung Suk; Kim, Hyun Su
CORPORATE SOURCE: R&D center, Cheil Foods & Chemicals Inc., Kyonggi-do, 467-810, S. Korea
SOURCE: Journal of Biochemistry and Molecular Biology (1996), 29(3), 266-271
CODEN: JBMBE5; ISSN: 1225-8687
PUBLISHER: Biochemical Society of the Republic of Korea
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A recombinant human erythropoietin (**EPO**), expressed in Chinese hamster ovary (CHO) cells, is glycosylated at Asn 24, Asn 38, Asn 83, and Ser 126. After release of the N-linked carbohydrate chains by peptide-N4-(N-acetyl-β-glucosaminyl)asparagine amidase F, the oligosaccharides were analyzed by FACE (Fluorophore-Assisted Carbohydrate Electrophoresis). The O-linked carbohydrate chain was separated by